Advancing Health Equity Across the Spectrum: Optimizing Biomarker Usage in Non-Small Cell Lung Cancer

CMEO Podcast Transcript

Monica E. Peek, MD, MPH, MSc:

Hello and welcome. My name is Dr. Monica Peek. On behalf of CME Outfitters, I'd like to welcome you and to thank you for joining us for today's CME BriefCase entitled, *Advancing Health Equity Across the Spectrum: Optimizing Biomarker Usage in Non-Small Cell Lung Cancer*. This activity is supported by an educational grant provided by Johnson & Johnson.

So, my name is Dr. Monica Peek and I'm the Ellen H. Block Professor of Health Justice. I'm also the Vice Chair for Diversity, Equity and Inclusion in the Department of Medicine at the University of Chicago. I've been a primary care physician for more than 20 years, screening for various types of cancer and walking patients through their journey when they get diagnosed with cancer. I'm really thrilled to be joined today by one of my colleagues, who is an esteemed colleague, Dr. Narjust Florez, as we talk today about a very important issue that affects many of our patients. Dr. Florez, or Dr. NJ, would you introduce yourself?

Narjust Florez, MD, FASCO:

Yes, it is my pleasure to be here, Dr. Peek, Monica. I'm the Associate Director of The Cancer Care Equity Program, the Co-Director of the Young Lung Cancer Program at Dana-Farber Cancer Institute, Assistant Professor of Medicine at Harvard Medical School, and Associate Editor for *JAMA Oncology*. I think this subject is extremely important, not only for young patients but for all patients because the diagnosis of lung cancer doesn't stop. Histologic subtype biomarker testing is essential.

Monica E. Peek, MD, MPH, MSc:

Absolutely. I'm super excited about the topic today.

Narjust Florez, MD, FASCO:

So, let's talk about what a biomarker is and the different types of biomarkers. A biomarker, I want our audience and learners to see it as the fingerprint of the tumor. That's what allows us to understand the tumor at a deeper phase, a deeper level. When you have a diagnosis of lung cancer, in this case we're talking about non-small cell lung cancer, we first have the histologic type. Is it squamous or non-squamous? And from the non-squamous, then they get classified as adenocarcinoma, large cell, and other subtypes. And even adenocarcinomas have other subgroups. They can be papillary. They can be mucinous. But that is a way to see the tissue to stains. Biomarkers can help us understand what precipitated the cancer in case of patients with driver mutations, what other risk factors the patient may carry to their family or they carry for other malignancies. Those are germline biomarkers or testing results. And then, we have the ones that will help us guide treatment.

Today we're going to focus on the ones that will help us understand the tumor and guide treatment. We're not going to be talking about germline testing. We're going to talk about somatic mutations of biomarkers that are acquired and they're seen in the tumor more than the DNA structure of the patient himself, herself, or non-binary. We define what a biomarker is. It's that fingerprint of the tumor. And there are biomarkers that are prognostic and predictive. This is very tricky, right? Because even in some cases we have biomarkers that are both. But prognostic indicates a patient's survival that is independent of the treatment received, because the

biomarker is an indicator of the innate tumor behavior. And we're going to talk about a few examples of one versus the other.

Predictive. This indicates therapeutic efficacy because there's an interaction between this biomarker and the type of therapy and the patient's outcome. Prognostic is what is characteristic of the tumor and predictive is, What do I need to select treatment that will help me understand how the patient's tumor will behave? Before we dive deeper on this, we need to understand that this happens to patients. The patients are not defined by their disease, so, avoid defining patients by the biomarker testing and defining by that, but still remembering how important it is. We talk about the fingerprint, and that is the base of personalized cancer care. When you're getting married, and I'm mentioning this, Monica, because I'm getting married in 2 months.

Monica E. Peek, MD, MPH, MSc:

Congratulations.

Narjust Florez, MD, FASCO:

There's a little reference in there. When you're getting married, you don't want to buy your wedding gown or wedding tuxedo, all the clothes that you prefer from the rack and just walk down the aisle. We all want the tailored dress the way we like, and that's biomarker testing in which we're able to tailor the care and we're able to tailor the testing, subsequent testing, and also the therapies. I haven't had yet a lot of resistance with that. Everybody likes tailored outfits. That has been good. It's also a good analogy of the key to the lock. The key is biomarker testing. You will understand what the patient needs to open that lock, which is the lung cancer.

Monica E. Peek, MD, MPH, MSc:

Those are excellent analogies. The bottom line is that these biomarkers are really critical in determining the best treatment that's tailored to patient care. And should providers wait for these results to determine a treatment plan? And how does health equity play a role in all of this? Because I imagine that some of these might be very expensive, and some of them may not be covered yet. How would a primary care physician like myself go about thinking about biomarkers?

Narjust Florez, MD, FASCO:

I think I'm going to use what we have learned over the decades for breast cancer so we understand. We no longer say breast cancer. We say hormonal receptor positive, hormonal receptor negative HER2. The diagnosis of breast cancer is never complete unless you have hormonal status. And that's how we see lung cancer. We should see it like that. However, like you mentioned, Monica, health equity has a role here. Unfortunately, populations who live in rural areas, populations of color, and outside of the U.S. borders, they have limited access to biomarker testing. And we're going to talk a little bit more that in detail as our conversation continues. But there are significant disparities, unfortunately, for biomarker testing. We're doing better than 10 years ago, but there are still disparities. I think everybody should wait for biomarker testing because there are therapies that are not effective in certain types of lung cancers, so you don't want to put a patient on a therapy that's not effective. Also, if the patient gets put in the wrong therapy, it may also interact with the subsequent therapy.

So, it's not only about choosing treatment but also avoiding unnecessary toxicity. Like I have told my patients, none of my drugs do not come without fatigue. They all come with fatigue. They all come with some kind of lab abnormality. Unfortunately, we don't have the first cancer drug yet that doesn't have side effects. Biomarker testing allows us to pick the best treatment to reduce the risk of unnecessary side effects, and many of the side effects are long-lasting. So, yes, it's like hurry up and wait. You get diagnosed with lung cancer and now your doctor is telling you that you have to wait 2 to 3 weeks for the results. But it's worth it because there's a difference between taking a pill once a day or getting full-on chemotherapy, so a very different quality of life.

Monica E. Peek, MD, MPH, MSc:

One question I have is for places that are out, very rural areas. Can they send specimens to tertiary and quaternary medical centers for testing? Is that something that's possible?

Narjust Florez, MD, FASCO:

One hundred percent. And there are two things, let's break this down. For remote areas or small practices and in an ivory tower at Dana-Farber and Harvard, of course, I understand. I used to work in the Midwest. I used to be at Mayo Clinic, so I had a firsthand experience of what it is to have nothing for 200 miles around you. There are institutions that do external testing for one of the very well-known such as the Mayo Clinic where I trained. Samples can be sent there. And there are a lot of commercial platforms that are available all across the country that small, medium practices can get samples to for testing. And there are many things that can be done now. There's also mobile phlebotomy for liquid biopsies, and we'll talk about that in a little bit. But mobile phlebotomies come to the patient's house to draw the blood for liquid biopsies or cell-free DNA or circulating tumor DNA (ctDNA). The pandemic had many challenges but also many opportunities, and one of them was to be able to do this biomarker testing with liquid biopsy at the patient's home.

Monica E. Peek, MD, MPH, MSc:

Excellent.

Narjust Florez, MD, FASCO:

We didn't know we could do it until then. Always in medicine, something needs to happen so we can do it.

Monica E. Peek, MD, MPH, MSc:

Right, emergency sort of creates ingenuity. Let's think about this in terms of a patient case. We've just talked about how important biomarker testing is to guide clinicians in precision medicine. Can you present Mrs. B. to us today and how we can think about providers integrating guidelines into her care?

Narjust Florez, MD, FASCO:

Yes. Before we go to this case, just quickly, there are many, many targets in lung cancer. There are not only one or two. There are many, and they continue to evolve. Only this year, we have two new targets. Every year this list is becoming longer and longer to a point that approximately 55% of patients we non-small cell, particularly non-squamous, having a target mutation.

Monica E. Peek, MD, MPH, MSc:

Wow.

Narjust Florez, MD, FASCO:

So, I want our audience to know that it's not “fishing” because I often hear that, "Oh, I'm fishing for biomarkers." No dear, it's 55% of adenocarcinomas. You're most likely to find a biomarker than you're not. We need to eliminate that perception that it's like, "Oh, I'm fishing." No, no, you're not fishing. You're actually catching the fish with your head.

So, let's talk about Mrs. B. She is a 77-year-old female with newly diagnosed advanced metastatic non-small cell lung cancer. She had previous tobacco use. Unfortunately, she had a decline in her performance status that is related to the progressive newly diagnosed cancer. Given her age, she proceeds directly to empiric chemotherapy and supportive care. Let's break this down a little bit. First, we need to understand that when we address performance status we need to take into account the cancer. That's a more definable aspect. When we evaluate performance status, we really need to see the patient before the cancer and what are some of the changes that the cancer has made to the patient that could be reversible with therapy? A lot of patients can have very rapid responses if they have a mutation, so biomarker testing, quickly.

And one thing that I struggle with is empiric chemotherapy. I'm going to be very honest. This is not Dr. House. There is no empiric chemotherapy. I don't like that term because there are so many side effects, and after chemotherapy has been proven over and over again that the adverse effects of chemotherapy stick around, I have patients with neuropathy 4 years after the last dose.

Monica E. Peek, MD, MPH, MSc:

Yes, yes. So do I.

Narjust Florez, MD, FASCO:

So, this decision shouldn't be taken lightly. It's neuropathy, right? So, empiric chemotherapy, supportive care, always and forever. But empiric chemotherapy, this is not Dr. House. We need to find that fingerprint. All right, so what is the consensus? Who should get tested? Every non-squamous non-small cell lung cancer with Stage IB to a stage IV should get tested. And I'm going to simplify that one. 1B to IV, non-squamous should get tested. If you have any doubt, you test. That's the answer. If you don't know, test. Nobody will judge you for testing. And this is in National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), all the guidelines have this, and it has been more broad now because these biomarkers are also affecting therapy in early stage. This is no longer a stage IV. We have approved targeted therapy for epidermal growth factor receptor (EGFR) early stage, ALK, RET coming up, new trials. So stage IB to a stage IV.

And I do recommend broad molecular profiling. What is broad molecular profiling? That's full next-generation sequencing (NGS) instead of trying to do gene by gene. Why is gene by gene not a good idea? One, you are going to forget a gene. Clinic is so busy. I was just having a meeting with my team and I was like, "You need to remind me," because I'm in clinic, right? It's like a different time when you're in clinic. You're so busy, so it can be hard to remember. And we just talked about how two biomarkers have been approved in the last year. So, for the

general practitioner who sees melanoma, lymphoma, benign heme, it can be very hard to catch up. Lung cancer is moving too fast, and I only see lung cancer. And I have a podcast about lung cancer. So, NGS makes sure you don't have to remember. Second, it's more cost-effective. If we are worried about the financial toxicity with biomarker testing, NGS is actually cheaper in the long run than doing gene by gene.

Monica E. Peek, MD, MPH, MSc:

Yes.

Narjust Florez, MD, FASCO:

And third is tissue, because the lung cancer tissue is still the issue. Biopsies are not as easy as a breast biopsy or a colonoscopy. It usually includes some type of intubation, a high-pressure environment for doing these biopsies. So, you want to preserve as much tissue as you want, and NGS allows you to do that. And, finally, I do like NGS because it lets me know what other baggage the patient's tumor may have. What do I mean by other baggage? We have the biomarkers that helps us direct therapy. However, new data are showing biomarkers like STK11 and Kip1 provide resistance to immunotherapy, so those patients need dual immunotherapy. It's not only about selecting the drug. It's just understanding mechanisms of resistance. For example, for patients who are EGFR who have *RB1* and *TP53* mutation at diagnosis, they are 40 times more likely to transform down their journey, to transform to a small cell. And this incidence is going up because we're developing better drugs. So, NGS helps me understand the baggage. This is what I tell my patients.

And here I am again with my analogies. When you go on a date, you want to know the baggage of that person who's coming, right? You want to know if they have been previously married. Do they have children? What is going on? You want to know as much as you can before you go on that first date. That first date is the first-line therapy. That's what is so important, because 30% of patients with lung cancer do not make it to second line. So, picking the first-time treatment may be more important than picking your first husband, but I'm not going to get into that, a little controversy. So, moving forward, what can we do to optimize testing? I think it's very important to have a uniform pathway in the institutions, and that we do guidelines and testing, instead of having a million pathways that leads to gaps in treatment and that leads to health disparities. When we have institutional uniform pathways, it allows the patients to all get the same testing.

I think updating the staff about new biomarkers and new therapies is very important. We are in August and we have four approvals, two new biomarkers, and it's only August. That's a change of administration. Things can be very fast in lung cancer, so it's very important that we stay updated. In addition to that, it's very good to learn from mistakes and look for barriers. If you have a patient who has a very long wait for biomarker testing, it is very important to come back together as a team and ask, "What happened? Was it enough tissue? Do we only get fine needle aspirations (FNAs)? Did the sample not get sent to the right place?" It's always good to make sure that we as teams are accountable, because biomarker testing is cancer care, so we want to make sure. And open communication. I have to tell you, I speak to my surgeons more than I speak to my mom. Today, I already spoke to two surgeons. It's very important that we communicate. At Dana-Farber, we have live tracking, all the biomarker testing. Also, to avoid me emailing them every time, it's like, "Where is my tissue? Where is the biomarker testing?" So, those are a few tips on how to optimize biomarker testing.

Monica E. Peek, MD, MPH, MSc:

Excellent. This is such good information, because this information is coming out so rapidly. It's hard for an oncologist to keep up. And then for me as a primary care physician, there's no way, so to have this kind of update is really valuable. One of the things that you had just mentioned is that there's a lot of testing that may be underutilized just because we may not be able to keep up with the information and to try and have some way of institutionalizing these pathways. Narjust, can you share with our audience some of the data around under-utilization so we can sort of get a picture of where we are in this country?

Narjust Florez, MD, FASCO:

I'm happy to. Before I break down the data, I want to be clear that most of the data are only about ALK, EGFR, and PD-L1. And that's only a small percentage of the biomarkers.

Monica E. Peek, MD, MPH, MSc:

Yes. We had this wheel of millions of biomarkers. It was a lot. It's 55%. And they all have weird names and weird letters. I remember being a fellow and saying, "How am I going to remember all of this?" And I was a fellow.

Narjust Florez, MD, FASCO:

Yes. And then at that time, Monica, not today myself, there were only four of them. And in these national electronic health records databases, over 17,000 patients, only 67% of all patients and 77% of patients with non-squamous had ALK, EGFR, and PD-L1 tested within 90 days of diagnosis. So, 77% should have been 100%.

Monica E. Peek, MD, MPH, MSc:

Right.

Narjust Florez, MD, FASCO:

And I strongly believe that if we add the other biomarkers, that number will be lower than 77.

Monica E. Peek, MD, MPH, MSc:

Absolutely.

Narjust Florez, MD, FASCO:

And lower rates were associated with locally advanced, so stage IIIB and C, particularly patients who have squamous histology and patients who were Black or African-American. Something important about this data is that the database did not have ethnicity, so, potentially, Hispanics and Latinx were also not appropriately tested, because, as we know, there are many issues with data when it comes to ethnicity.

Monica E. Peek, MD, MPH, MSc:

Yes.

Narjust Florez, MD, FASCO:

Furthermore, Molecularly Informed Lung Cancer Treatment in a Community Cancer Network (MYLUNG) did a study of nearly a thousand patients in community practices and showed that 64% of patients with early-stage and 83% of patients with metastatic lung cancer had at least one biomarker. We're talking about one, right? And there are like 11 now, of which 36% and 17% had no testing. So that's like Mrs. B.'s empiric chemotherapy. No, no, no, no. That's so 2009. And 30% of patients with metastatic non-small cell lung cancer had results for at least nine biomarkers, so less than 50% have nine biomarkers, which is probably ideal. And only 37% of early-stage and 57% have the NGS that we just talked about. That is very beneficial. So, you're probably wondering, that's like homegrown, right? This is in the United States.

Monica E. Peek, MD, MPH, MSc:

Right.

Narjust Florez, MD, FASCO:

Is it the first, globally? Surprise, it is. I'm very proud to be a member of the International Association for the Study of Lung Cancer (IASLC) and a new board member. In 2024, we conducted the second IASLC global survey of biomarkers, and it's over 1,600 respondents in 90 countries. This survey is to doctors and providers, and 98% believed that biomarker testing significantly impacted outcomes. So, people know of it, though only 63% and 29% rank it highly important in late and early-stage. This is important because we have worked for the last, I would say, 15 years to improve testing in metastatic disease. Still, 64%, at best, and for early stages it's even more challenging.

Monica E. Peek, MD, MPH, MSc:

Right.

Narjust Florez, MD, FASCO:

Unfortunately, biomarker testing is not accessible in many low- to middle-income countries. A lot of the guidelines that we're working on are that it's better to test in tissue, then get genomic testing. So, what is this? We have certain biomarkers that can be tested with immunohistochemistry (IHC) versus PCR or NGS, in limited resource settings. I was just in Columbia and I told them it's better to have an IHC than to have nothing. Don't undermine the value of IHC compared to having nothing. We can do IHC for ALK, ROS1, for HER2, for example, and those tend to be cheaper compared to NGS when they may not be available. Like my grandma used to say, I don't know about your grandma, but I was raised by a Latina grandma and my grandma always told me, "There is always a way around." That has been very helpful for our career in academia because there's always a way around.

Monica E. Peek, MD, MPH, MSc:

These numbers are stunning. We've got so far to go. But you're right, we cannot let the current status quo keep us paralyzed. We have to continue to move forward. We have to think about your grandma's words and figure out a way around. Let's go back to our patient, Mrs. B., who's 77 and considered older. What do we know about

treating older patients with non-small cell lung cancer, and particularly in the setting of this new information that we have to learn about tailoring medication and therapies for people?

Narjust Florez, MD, FASCO:

Over 50% of patients who are newly diagnosed with non-small cell lung cancer are older than 70 and 50% are older than 80. These numbers are only expected to get higher in some departments, lower in some others. But, for example, today I had a patient where lung cancer is the third cancer she had. She survived breast cancer, she survived ovarian cancer, and now we have lung cancer. So, we are getting good with therapies. Our population is aging. This is not 1930 where people were dying of tuberculosis. Our population is aging, and it is more important to know that a lot of older patients were not included in clinical trials. I have a publication from 2017. I always talk about this publication as my number one, my first one-hit wonder if it sold. It was the first publication, I was a fellow, that goes on national attention, which showed that the majority of the patients going into lung cancer clinical trials are men and fit and young. That is not what walks in my clinic. That is not the reality. And all of them follow all the policies. I always tell my patients, "There was no transportation issues in the trial." So, patients who are geriatric have risks for certain organ damage, because like I told my patients, "Age is a number, but we cannot forget that your bone marrow is 75 years old. We cannot forget that your kidney is 75 years old," and they're also very likely to have polypharmacy, which is very common, unfortunately. And actually, that was my thesis for medical school, polypharmacy in the older adults.

Monica E. Peek, MD, MPH, MSc:

My bread and butter of the patients that I treat, they have hypertension, they've got diabetes, they've got dyslipidemia, they have all of these problems, and then they get cancer on top of that.

Narjust Florez, MD, FASCO:

And on top of that, you add the supplements that we don't know how they interact.

Monica E. Peek, MD, MPH, MSc:

Right.

Narjust Florez, MD, FASCO:

But it's part of our culture. My family are all physicians, but my grandma was a grandma before. She was always grandma first, physician later. And it's also part of culture. However, this may sound repetitive, chronologic age is just a number. I have patients who are less than 50 who have a very limited performance status. And I have a fabulous 85-year-old right now. I don't have any other words to describe this woman but fabulous. And everybody was afraid. I sent her to the geriatrician because I do geriatric assessments on my patients, particularly early stage. I don't want to send a patient to surgery, and then we had complications, to assess the patient holistically because age doesn't matter. And this fabulous 85-year-old cruised through chemoimmunotherapy, she went to surgery, and after I met her, she had a complete response. She had a margarita that day because she didn't need more treatment.

So, age is just a number and it's not something that we say to make her feel better. It's because holistic assessment of patients is what actually will determine the next step. I have a 32-year-old and cancer has done awful things to her, and I have this fabulous 85-year-old who will give anybody a run for their money. So, assessment of patients holistically is what is the right thing to do for all patients. And one of the important things about targeted therapy and biomarkers is that biomarker testing allows us to give patients more tolerable therapies. It's very different to be taking a pill once a day than getting chemotherapy and you will lose your hair. We do know that platinum-based therapy tends to be more toxic in patients who are age 70 to 79, even the ones who have good performance status. So, it's higher risk of death and hematologic complications, and we talk about the bone marrow, renal complications, and neurologic complications.

And, Monica, as a primary care doctor, you probably have seen this. We have these patients who are 70, 79 years old, and they have been doing well. But as soon as you take them out of the environment, because of a new lung cancer, all of these neurologic deficits that we're not aware of, to the patient, the family, the spouse, and just a little thing tips that over. That's why targeted therapies are better-tolerated than chemotherapy and also better quality of life. They also have less interactions.

Immunotherapy. There's actually a study done by the FDA that was presented at ASCO in 2023 that showed that patients who have a high PD-L1 biomarker, so meaning higher than 50%, and even patients higher than 90%, older patients, older than 75, they have better outcomes than if you give them chemotherapy plus immunotherapy. So, that biomarker makes the difference. I do infusion every 6 weeks or infusion every 3 weeks without the risk of renal damage. So, biomarkers are so essential for the treatment of geriatric patients. It shouldn't be only for young patients. Everybody deserves biomarker testing.

One of the things that we need to take into account is that a lot of geriatric patients may have a past medical history of tobacco use. Tobacco use significantly increased and then we saw a drop. That the patient has a previous tobacco use history should not be a contraindication for biomarker testing. We have biomarkers that are associated with tobacco use that had pills like BRAF, Exon 14, KRAS G12C, which is actually the most common biomarker. So, smoking history should not be exclusion criteria. And even the opposite, I think we should look for biomarker testing in the older population so we can have better options for them. I think special attention should be taken into account not only about biomarker testing but about the side effects of chemotherapy are no joke.

Monica E. Peek, MD, MPH, MSc:

Yes. This is super interesting just how the history of smoking, the age, how all of these things can change with this additional information that we can get with biomarkers. So, what are our key takeaway messages from our first case?

Narjust Florez, MD, FASCO:

I think the key takeaway is that age should not determine the choice for biomarker. And also no performance status either. I have seen many times how appropriate biomarker testing has helped patients improve to a point that they're not who they used to be with their cancer diagnosis prior to starting therapy within 6 weeks. This is the magic of biomarkers because you're able to find a therapy that provides responses that we never have seen before. I have a patient just a few weeks ago, ALK-positive, older patient, and I started targeted therapy. In 6

weeks, the patient came without oxygen, without a wheelchair, and no cane. He was back to hitting the balls at the driving range.

Monica E. Peek, MD, MPH, MSc:

Oh my goodness.

Narjust Florez, MD, FASCO:

That's the difference. I never have seen somebody who goes to chemotherapy and 6 weeks later comes back saying, "I feel great."

Monica E. Peek, MD, MPH, MSc:

Right.

Narjust Florez, MD, FASCO:

Hardly anybody.

Monica E. Peek, MD, MPH, MSc:

It's like a miracle.

Narjust Florez, MD, FASCO:

Yes. So, that's the key. It's the importance. And sometimes, I just have to bring this to your attention, we don't have enough tissue. I often get asked by oncologists in the community, "Should I go for more tissue?" I'm like, the answer is always "Yes" because you may have enough tissue for DNA biomarkers and you may run out of tissue for RNA biomarkers. The irony of that is that DNA biomarkers are always run first. The best therapies are actually the RNA biomarkers, ALK, ROS1 have the best overall survival, the best outcomes. So, yes, the answer is always, "Go and get more tissue if possible."

Monica E. Peek, MD, MPH, MSc:

Excellent. This was super helpful in learning just all of this but also thinking about the impact of basically age bias and thinking about who might qualify for some of the treatments and therapies for lung cancer, for non-small cell lung cancer, and the critical role for education of providers as well as patients, and engaging all members of the treatment team. I want to shift our conversation a little bit to thinking about other kinds of biases that we may have and other social drivers of health that may impact who gets care, how they get care, et cetera. Can you talk a little bit more broadly about social drivers of health and how that may impact lung cancer treatment?

Narjust Florez, MD, FASCO:

I think social drivers of health are as important as biomarker testing. I think they're both linked because where you play, where you work, and where you live influences your entire experience. We just did a large study in which we interviewed African-American patients with lung cancer, and their commute to the cancer center affected their treatment choices, their participation in clinical trials. So, as important as the history of

hypertension and diabetes is, what is your health literacy? How far are you from me? What are issues with the insurance? Who cares for you at home? Who do you have to care for at home? Because many of our patients are also caregivers. All of that affects the cancer continuum, and it's directly related to biomarker testing. Because we know that patients who are in low settings, like low-income settings or limited-resource settings, they're less likely to have biomarker testing. So, where we live, where we work, where we play is as important as the biomarkers, because how does it matter that you have a PD-L1 or 100% if you don't have a way to get to the cancer center for the infusion, right?

Monica E. Peek, MD, MPH, MSc:

Right.

Narjust Florez, MD, FASCO:

That's why I ask all my patients the questions.

Monica E. Peek, MD, MPH, MSc:

Right, all of the infrastructure that is available to those who have the financial resources and who don't have the responsibility that comes for those who have limited resources. So, can you talk a little bit about the actual association between some of these social drivers and the prevalence of lung cancer itself?

Narjust Florez, MD, FASCO:

Lung cancer is one of the cancers that's directly associated with poverty. I'm going to use the Appalachian area as a great example. The Appalachian area in the United States has one of the highest incidences of lung cancer but also has one of the highest incidences of poverty and limited resources. Many of the towns are minors' towns, so there tends to be a lot of generational behaviors. "My father smoked. I smoke." And in many of these jobs, the only break that many of these employees have is when they go for a cigarette. That whole driver in the Appalachian area is learned behaviors, limited resources, limited health care, and limited job opportunities that actually drives the patients to increase tobacco use. We also know that for non-smokers or non-tobacco users, radon is our number one risk factor. What happens with radon? What about people who live in subsidized housing? In many states of the United States, we did a study at the University of Wisconsin, but in Wisconsin in general, there are no real rules for Section 8 housing about radon testing. Many of these properties may have never been tested for radon or were tested when Reagan was president and they never have been tested again. So, that is linked to property and that's linked to lung cancer for tobacco users and non-tobacco users.

Monica E. Peek, MD, MPH, MSc:

Yes. So many of the toxins and things in our water and our air and our earth are disproportionately burdened on poor populations. There are many environmental linkages between cancer and poverty, this being a great example of people in Appalachia. I want to have us translate this into another patient case. So NJ, can you talk about our next patient?

Narjust Florez, MD, FASCO:

Of course. We have Mr. L. who's a 60-year-old, African-American man with newly metastatic non-squamous cell, non-small cell lung cancer. He receives disability income and has Medicaid or state insurance. Due to the cost of travel constraints and lack of reimbursement for testing, single gene testing for EGFR, ALK, ROS is performed. Testing results are negative and immunotherapy is started. The issues I have with this, I just want to break it down first, is that first, you use a lot of money. We're talking about constraints, right, to do EGFR, ALK and ROS, but no PD-L1. So, biomarker testing didn't really guide it, the PD-L1, and in some patients if PD-L1, which is a biomarker, is not high enough, immunotherapy is not enough and they need chemotherapy plus immunotherapy.

Monica E. Peek, MD, MPH, MSc:

So, already, you're seeing all kinds of things that are wrong with his care. One of my questions was, my official question is, How are these social drivers and biomarker testing playing a role for this patient's care? Can you talk about insurance coverage for biomarker testing? Does it cover some? None? What do we know about that?

Narjust Florez, MD, FASCO:

Well, I think, unfortunately, insurance coverage has become so complex. It's very hard to make a blanket statement. Even the same company, even the same patient, I have the pleasure and the challenge of treating family members both diagnosed with lung cancer, and both on the same health plan where one was the policy holder and the one was the dependent. And I was like, "The coverage should be the same."

Monica E. Peek, MD, MPH, MSc:

Right.

Narjust Florez, MD, FASCO:

No, it wasn't.

Monica E. Peek, MD, MPH, MSc:

Wow.

Narjust Florez, MD, FASCO:

It has become so complex, and they're putting so many obstacles to providers to get things approved. I do think it's like, "Let's put as many obstacles until the doctor gives up on this," right?

Monica E. Peek, MD, MPH, MSc:

Yes.

Narjust Florez, MD, FASCO:

Like I have told my patients, "I'm not pushy, I'm persistent." I think it is mandatory for most insurance to cover. They may request a peer-to-peer or they may request some required...but a lot of insurance needs to follow the

NCCN guidelines. What's clear in the guidelines is that for stage 4 non-squamous patients need to get biomarker tested. What is tricky here is which biomarker testing, right? This patient only had three. Do you fill the criteria? No, but in theory the insurance covers biomarker testing, so it should be mandatory. I think challenges are placed to the providers. And sometimes, patients get these bills after you get the biomarker testing, and they're like $5,000, $6,000. And it takes a lot afterwards to get it covered some way. But like I tell my patients, "Do not pay anything until they told us you have to." Because a lot of patients with cancer, and this is something very unique that I want our learners to know, feel the need to pay because that's what they have to do. I think it's very unfair. They're dealing with a lot, and a lot of them pay, they sometimes tell me. But over time we talk to patients and say, "You tell me. You tell me if something comes. Send me a picture and the patient gateway or whatever the letter is." Because, some of these letters are very scary.

Monica E. Peek, MD, MPH, MSc:

And I imagine that particularly for families with limited resources, they're imagining that, "I have cancer, I may not survive this. Let me try and pay these bills so that I don't have to pass them on to my kids."

Narjust Florez, MD, FASCO:

That is so true. There is nothing more noble than a patient with cancer.

Monica E. Peek, MD, MPH, MSc:

Right.

Narjust Florez, MD, FASCO:

And if you're a woman and a woman of color with cancer, everybody's priorities are on top. It is important that we teach patients that, like my grandma said, just going back, "There's always a way around."

Monica E. Peek, MD, MPH, MSc:

That's right. That's so important that people have this kind of advocacy, because so many people are hounded by bill collectors and medical debt. And to have someone who is in the healthcare system saying, "Ignore that because we're going to fight that. You worry about your care. We're going to push for this," to help to prioritize and to let them know that it's okay. I think that is hugely important.

Narjust Florez, MD, FASCO:

Yes.

Monica E. Peek, MD, MPH, MSc:

Thank you for all that you do.

Narjust Florez, MD, FASCO:

One thing before we move on, Monica, is I think health literacy is really related to biomarker testing. I think patients have limited health literacy and I do not believe in putting the responsibility of biomarker testing on patients.

Monica E. Peek, MD, MPH, MSc:

Absolutely.

Narjust Florez, MD, FASCO:

Because a lot of the teaching is like, "Oh, you need to ask your doctor." No, no, it's your doctor's job to do that. We don't need a patient who just got diagnosed with cancer to have more to-do lists, in my opinion.

Monica E. Peek, MD, MPH, MSc:

Right. All right. Do we want to go back to our case and Mr. L., or is there anything else you want to talk about before we come back to him?

Narjust Florez, MD, FASCO:

I think we can come back to Mr. L. Our learners need to know what happened. Due to implicit bias or unconscious bias and false assumptions about limited access to expensive therapies, he may not be able to access targeted therapy, drugs or clinical trials. He has significant delays in biomarker testing and, as we talked about it, he only had EGFR, ALK and ROS. Then, immunotherapy was started. However, later it was found that the patient had a HER2-positive tumor. The issue with that is that the first-line treatment was wrong, and patients with HER2 disease tend to have a lot of progression in the central nervous system, and when they have disease progression it can be catastrophic. Very unique type of lung cancer.

Unfortunately, this patient's life was called short by the lack of biomarker testing. We have oral therapies for HER2 that was just approved 14 days ago, and we have intravenous therapy for HER2. Immunotherapy alone is not enough for these patients. Immunotherapy can be part of the regimen but alone is not enough. So, we cut this patient's life short. It is unfair. We have done biomarker testing and honestly it's just bad medicine. Because beyond the altruistic goals of doing the right thing, it's about being the right doctor and the right provider. It is not only the doctor. I think everybody's involved in a patient's care. Nursing, nurse practitioners, physician assistants, they're also part of the care. And sometimes it's just one voice that is needed, like, "Oh, what about Mr. L.'s HER2 status?" That's IHC, which is cheap. That is my summary for that case. Unfortunately, this story for Mr. L. is not rare. It happens every day.

Monica E. Peek, MD, MPH, MSc:

I can imagine. We look at the statistics for health disparities, but each of those statistics is a story, and a story that if we heard about them, we can easily see how they would play out. And most of them are not horrible cases of whatever. They're like, oh yeah, yeah, these little things that just add up to be something that can kill someone. Which gets to our next point of having all eyes on the patient, of having a team-based approach where multiple people are empowered to say, "Hey, what about that HER2 status?" And social workers involved,

and the primary care physician, because a lot of patients will go see their oncologist and then come back to me and say, "What do you think about this?" And I'm like, "I'm not the oncologist," but I'm the one they trust.

So, having a team-based approach is just as important as we think about these social drivers, as we think about biomarker testing. I've got to make sure that I'm up to date but also thinking about how we do team-based care. One of the most important things is not just our commitment to evidence-based practice but our commitment to making sure that we are all on the same page as far as having clear channels of communication, that we're all committed to a collaborative approach and hearing each other, that we are all committed to not just us being a team but us having the patient at the center of that team, and that the patients and their family and their social support network is included in these decisions.

That is how we make this whole thing work, that we make sure that balls don't get dropped, that patients don't fall through the cracks, that we adhere to guidelines of care, and that disparities don't continue to happen no matter if someone's living in a rural area or that they have insurance that may want to make us do 7,000 paperwork faxes to get approved. Working as a team can help with our best patient outcomes.

We are almost out of time, but I'm going to try to summarize what we've talked about with some SMART goals, and then I'm going to have you tell me what I've missed. SMART goals are those that are specific, measurable, attainable, relevant, and timely. These are the major points that I want our audience to take away from our presentation today. The first is to implement reflex testing protocols. That ensures that all eligible patients receive comprehensive biomarker panels, removing the need for patients to initiate them or providers to initiate them, one-off testing, that there's a whole comprehensive panel. Two, that we ensure that every patient who has non-small cell lung cancer is eligible for systemic therapy, who is eligible is not denied this comprehensive biomarker testing due to misconceptions or operational barriers or things about insurance. And then, three, to promote a team-based approach to ensure that testing is performed early and the results are available to inform therapy choice. NJ, is there anything that I missed or anything else that you want to add?

Narjust Florez, MD, FASCO:

I don't think you missed anything. I think I would like to add that tobacco use history and age should not be factors that we preclude biomarker testing.

Monica E. Peek, MD, MPH, MSc:

Absolutely. All right. I want to remind our audience that this activity and a wide variety of activities and resources about non-small cell lung cancer are available on the CME Outfitters website and that today's CME BriefCase is just one of a series of activities that can be found on the Health Access and Social Responsibility Hub on the CME Outfitters website. I hope that you'll check out the other activities in the series. All of them are fabulous. To receive CME or CE credit for this activity, participants must complete the post-test and evaluation online, so please do that to receive your credit. You'll be able to download and then print your certificate immediately upon completion.

So, I'm Dr. Monica Peek. I want to thank you, our audience, for your continued commitment to ensuring that all patients receive the best care. Thank you, Dr. NJ Florez, for joining me today. It really has been a pleasure. I thank you for all that you do, for your patience, for all of the education that you continue to provide around the country, for joining us today, and for being a beautiful human. Thank you so much.

Narjust Florez, MD, FASCO:

Thank you, Dr. Peek. And thank you to CME Outfitters for continuing to talk about equity and access, because regardless of what happens, that is still a priority.

Monica E. Peek, MD, MPH, MSc:

Great. Thank you so much. Have a great day, everyone.

