Transcript Details

This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/cme/an-update-on-biomarkers-in-nsclc-clinical-management/16387/

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An Update on Biomarkers in NSCLC Clinical Management

Announcer Open:
Welcome to CME on ReachMD. This activity, titled “An Update on Biomarkers in Non-Small Cell Lung Cancer Clinical Management,” is provided by Partners for Advancing Clinical Education – PACE – and supported by an educational grant from CGEN. Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements, as well as the learning objectives.

Dr. Sims:
Well, welcome again to our afternoon sessions, and this is a great presentation I am looking forward to. It’s an update on biomarkers and non-small cell lung cancer clinical management, and a great speaker, Rasheda Persinger, who is the lead nurse practitioner in the Division of Medical Oncology at Johns Hopkins in Washington, DC, and I know she will bring a lot to this presentation for us today. These are her disclosures. And I’ll remind you of our learning objectives, which are to identify actual biomarkers and their impact on non-small cell lung cancer; and to integrate recommended approaches to biomarker testing into the management of these patients; and to utilize the results of biomarker testing to identify optimal treatment strategies for patients with advanced non-small cell lung cancer.

Ms. Persinger:
Thank you so much, Terran. Thank you for everyone that has logged in. Let’s get right into it, because we have a lot of information to cover in a short amount of time. So, Ie – lung cancer remains a major global health burden. What we do know is lung cancer is one of the most common cancer, and is the leading cause of cancer deaths in the U.S. and worldwide. As you can see, the new cases are, in the U.S. there’s over 200,00, globally over 2 million in 2020. The deaths in the U.S. was greater than 127,000 in 2023, and globally 1.8 million. So this is really something that needs to be, you know, talked about and discussed. So, the 5-year survival rate is overall 22.9%. Metastatic – and when there’s a metastatic diagnosis, that’s even lower. So non-small cell lung cancer accounts for between 80% and 85% of lung cancer.

So this is a great chart. It’s approximately 50% of patients with advanced non-squamous, non-small cell lung cancer, have a driver mutation, targetable by FDA-approved agents. And so, this is a wonderful pie chart that kind of breaks down each of those mutations, along with its respective FDA-approved product.

So why do we perform biomet – biomarker testing in non-small cell lung cancer? We know from many studies that patients who get chemotherapy, as opposed to targeted therapy specific to their driver mutations, do much worse. And that’s what this graph kind of shows us over here. It shows that the overall survival by receipt of guideline-recommended therapy. When patients were placed on their private therapy, they had a overall survival of 18.6 months, versus if they were – did not receive that therapy, just had a broad space chemotherapy, despite having a driver mutation, that number was lower. 11.4 months was their overall survival.

Dr. Sims:
Alright. Here’s our case study. John, a 65-year-old gentleman, presented to primary care complaining of dyspnea, persistent cough and intermittent pain in the left side of his chest. After a chest x-ray revealed a lung mass, and a biopsy confirmed adenocarcinoma, he was referred to an oncologist. He’s a never smoker, however, he had childhood exposure to secondhand smoke. No palpable masses or visible lesions on physical exam, and his ECOG performance status is 1. The diagnostic workup included a PET imaging, which revealed extensive tissue involvement, greater than 3 cm, and a brain MRI showed one brain metastasis at 0.5 cm. The diagnosis of stage 4 adenocarcinoma was arrived at.

Ms. Persinger:
So, let’s just remember. Remember that first slide I showed you, had all of those different mutations, right? And in this patient’s study, we’re looking at a metastatic, stage 4 patient. But are we testing? I think that polling kind of gives us some equal.Are we really testing

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like we should be? This is a study, it's called the Mylo Consortium data, which polled out 300 – 3,474 patients in the U.S. oncology network through the years of 2018-2020. 74% of those patients were adenocarcinoma, and so when we looked at this, and looked at the overall testing of next generation sequencing, what we saw is that when patients were in non-squamous – so non-squamous is that adenocarcinoma, there were only 39% of patients that had next generation sequencing. That means, testing all of those biomarkers that have an FDA drug therapy for, and that's what this slide shows us, that the next generation testing over time, with overall population, though it isn't proven, it's still not where we are. Yes, we have that single assay of people doing an EGFR, or maybe Alpha-1, but again, remember that first slide, with all of those new patients. We cannot, you know, risk missing a mutation because we just did single assay.

So biomarker testing in advanced non-small cell lung cancer, and this comes out of the NCCN guidelines. As you can see, when we look at non-squamous – remember, non-squamous are those adenocarcinomas. And it's listed there, all of those mutations that have a derived, FDA-approved drug. So the importance of getting that next generation – that – what the NCCN guidelines states is that broad, molecular testing, preferably with NGS-recommended, to use least amount of tissue. And then, obviously, PD-L1 by IHC. And then, squamous – even in squamous, because you have some of those patients that fit those characteristics that consider molecular testing. Raw molecular testing is preferably, with NGS-recommended, to use, again, least amount of tissue. And again, PD-L1 by IHC.

So, what is just – I want just to really drive home is that order biomarker testing, preferably NGS, and make sure that we identify any actual mutation in all patients with advanced, non-squamous, non-small cell lung cancer. Consider it in non-small – in squamous non-small cell lung cancer. Thank you.

So now we're going to talk about biopsy for biomarker testing a little bit more. So, tissue from the primary tumor or the metastatic site – equally suitable. It's considered the gold standard for biomarker testing. Lung cancer biopsies are less cellular than other solid tumors. Need about 10-20% of viable cancer cells as samples, for reliable results. Lung tumors can be heterogeneous in origin, so remember that. Bone biopsy potentially is suboptimal, due to the decalcification and degradation of DNA, but new methologies are evolving. You also have liquid biopsy, which is just cell-free DNA and plasma, are another option. But, look at this liquid plasma. I know everyone has probably heard of it. It's a blood sample that's containing cell-free DNA from multiple sources, including DNA shed from its – from tumor. So in simplistic terms, you have this abundance of cancer cells being pushed into the bloodstream and you get this blood sample. And when do we use liquid biopsy? Plasma first approach is for inadequate or no tissue biopsy. If negative, we biopsy for tumor tissue, and a sequential approach is where you get the tumor tissue. It's adequate for genal typing but then you follow it with cpDNA testing, only when results from tissue are incomplete.

Then there's a complementary approach. Increases the rate of biomarker detection. And then, definitely, if there's a resistance to TKI. There's advantage, right. Advantage is that it's minimally invasive, may overcome tumor heterogeneity, but there are some limitations, which include the sensitivity is only 70-80%, specificity is near 100%, negative result is noninformative and not – and it cannot assess histology or PD-L1 status.

Dr. Sims:
So, here's our case again. John's molecular testing by NGS indicates that his tumor is driven by an EGFR ex-19 deletion mutation. I wonder if, Rasheda, you'd like to comment on this slide.

Ms. Persinger:
So, this is just – it's a printout that we typically get, depending on your institution, support dependent on what course you use for getting this interrogation of the tissue, but this is just showing you in the alteration, what alteration is identified. It always usually tells you the cell freeing DNA, percentage of where it was noted, and then it gives you that associated FDA approval therapy, and then, along with the clinical trial. So this is basic, and all – at the bottom will give you different variants, and so forth, that may or may not be utilized at that time, but maybe in the future.

Dr. Sims:
I'll turn it back to you, Rasheda.

Ms. Persinger:
So, EGFR mutations – I think that anybody that knows lung cancer is probably very familiar with EGFR mutations. There is more common, but not exclusively, to never or minimal smokers, East Asians and women. Its practical mutations make up the majority, and that's that Exon-19 deletion and that Exon-21, or you may have heard of it as L-858R. There are some atypical and uncommon EGFR mutations, including the G-719X, the L-816-1Q, and the S768I. Some are sensitive to traditional EGF inhibitors, some are not. And of course, there's more studying needed. The uncommon EGFR mutations is in the pie graph that is shown there. I'm not going to go over the Exon-20 insertion, because we'll talk about that a little bit later.

So, when we look at biomarker-directed therapy in advanced non-small cell lung cancer, the classical mutations – these are a different

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generations, right? That first, that second, that third generation. And as we came down to that – this fourth generation, the thought is that there are less – or not the thought, the literature, the studies show that there are less side effects that we could see, in terms of rating when we got to that fourth generation of drug. And so, it is FDA-indicated in first line metastatic non-small cell lung cancer, with L858R or Exon-19 deletion. Subsequent lines of metastatic, if you harbor that resistance strain of P790M, at the progression of, maybe what they were initiated on that first or second generation of drug.

So, the FLAURA trial was very monumental. This trial looked at osimertinib versus first generation TKIs, that showed that it was improvement in the PSS for patients with advanced EGFR positive, non-small cell lung cancer, with CNS met, which is important, right?

Because we all know that patients, more than often in that stage 4, there is this presentation of brain met, or at some point they will brain met. So they included patients that had CNS met, and what is shown is that osimertinib improved overall survival in PFS and overall patient cohort versus gefitinib or erlotinib. The overall survival, as you see there, is noted in terms of the hazardous ratio, and when we looked at this graph, it showed us a PFS in patients with CNS met, so that's important, right? That's one of the things that we really want to look at. When we looked at that, the median PFS was 15.2 in osimertinib arm, and 9.6 months in the standard of care – those first generation TKIs. So this was huge, and showed that there was really good CNS penetration there.

So when we look at phase 3, which was the ADAURA trial update. So this is using osimertinib in those patients with early stage disease. So these are patients that are post-surgical resection. They were known to harbor that EGFR mutation – Exon-19 or Exon-21. And so what this was is that international, randomized, double blinded, phase 3 trial that showed that there was a PFS in overall population, regardless of the stage when we look at early stage - stage 1B, stage 2 and stage 3A. And what we see is the breakdown of over even and we did a 2-year analysis, a 3-years and a 4-years. Still showed a good PFS and approval. And so, when we looked at the median DFS in months, the osimertinib arm was 65.8 months versus placebo, meaning that they did not get the kind of therapy. They may or may not got adjuvant chemotherapy. That arm was 28.1. So, FDA approved in December of 2020, for adjuvant treatment of adults with stage 1B, 3A and – stage 1B through 3A, EGFR positive, non-small cell lung cancer. Both tumor resection plus or minus adjuvant chemotherapy.

So, when we – again, when we're looking at the dosing and the side effects, same thing in the adjuvant setting as well. It's 80 milligrams in the adjuvant setting, you're doing it for 3 years versus in the metastatic, where it's until disease progression or poor tolerability. A frequent side effect that we see is diarrhea, rash, dry skin, nail toxicity, stomatitis, fatigue, decreased appetite. Some of those grade 3 or greater side effects, we just need to keep an eye on, is that decreased appetite, diarrhea and the QT prolongation, and I highlight that because we know in our oncology patients, they tend to be on other drugs that can cause QT prolongation. One that comes to mind is Ondansetron.

So I said we're going to go back in terms of Exon-20 mutate insertion, which is an EGFR mutation. So this is the follow study, imabatinib, in EGFR Exon-20 insertion-positive advanced non-small cell lung cancer. Co-platinum, so remember, I said in that second line. So this is best overall response by Exon-20 insertion free, and it kind of just broke it up, and – dependent on the hillicate region, mirror, their loop, the far loop and not detected by cpDNA, but they still derived a response.

And so this shows you the breakdown, their overall response rate, as it related to the different region that they were in.

So when we look at the CHRYSALIS study even further, in EGFR Exon-20 is – the 20 insertion positive advanced non-small cell lung cancer, post platinum again, second-line therapy. When we look at the PFS, and the median PFS overall was 6.9 months, and then the overall survival was 23 months. And you can see there at the breakdown, as it relates that the overall response rate was 37%, efficacy consistent regardless of prior therapy or response to prior platinum-based chemotherapy. 13% of patients remained on therapy, with split PS and a median treatment duration of 2.6 years.

So when it – let's look at the side effects, right? And what is that AE, when we talk about this imabatinib. What I see is that is a 90% chance of happening is an infusion-related reaction. Commonly recurs during the first infusion. As you can see there, 93% of cases did not affect the ability to receive subsequent treatments. And we're just managing as we normally would manage it. One of the things in this is that you do premedicate, with glucocorticoid on week 1, day 1 and day 2. We premedicate with acetaminophen and diphenhydramine with all doses. Split the doses of the first infusion is over two days, and if IR is suspected, interrupt the drug and give supportive medication as needed. Some of the other side effects that we see – the all gray – you see that rash, we see that paronychia, we see that stomatitis and pruritis. If there was a met-related mutation, or met-related side effect that we saw was lowering the albumin, and that peripheral edema. And then, that gray – two or more that didn't happen as much but is worth mentioning, is that there's the rash and the paronychia there.

So, anti-tumor activity of mobocertinib. In previously-treated EGFR Exon-20 insertion positive, metastatic, non-small cell lung cancer suggests that note the imbatinib is intravenous, right? Mobocertinib is oral, and so when we looked at this, and we looked at the data that

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supports this, the confirmed overall response, that there was 28 in the cohort arm and the plain cohort was 25. When we looked at the median DOR was 15.8 in the PPP cohort, and not reached in the ECLAIM. When we looked at the confirmed overall response percentage, when we looked at the PPP cohort, it was – the CR was less than 1, the PR was 34, and the median DOR in months was 13.9. The confirmed BCR was 78. When we looked at the EXCLAIM arm, the median DOR was 11.2 and the confirmed BCR was 75.

So, the TREs, as we – as it relates to mobocertinib in greater than 20% of patients, as you can see with this graph here, shows that the biggest one is the rash.

We see the paronychia, that decreased appetite, there is some of that diarrhea, but then the dry skin, the vomiting, the increased creatinine. When we looked at the EXCLAIM arm, the rash was again up there at the top, paronychia, decreased appetite and dry skin. Diarrhea management – begin antidiarrhea at the first occurrence, and increase fluid and electrolyte intake. Withhold drugs until resolution to grade less than or equal to 1. For intolerable, recurrent, grade 2-3 and first occurrence of grade 4 diarrhea, discontinue for recurrent grade 4 diarrhea. And just as a reminder, proactive mitigation and management of diarrhea associated with mobocertinib in patients with a EGFR Exon-20 insertion-positive advanced non-small cell lung cancer may reduce its severity. So there's very important to have that ongoing dialogue, that open communication with the patient.

Dr. Sims:
Okay. So here's our case study. Marie, a 60-year-old with non-small cell lung cancer, with KRAS G12C mutation after first-line therapy. She has a 40 pack-year smoking history, and was diagnosed with metastatic lung adenocarcinoma after she presented with back pain and shortness of breath. She had biomarker testing, and showed PD-L1 by IHC was less than 1%. Her NGS – her KRAS mutation was seen, and she received first-line pembrolizumab and carboplatin/pemetrexed, and now has disease progression.

Ms. Persinger:
Alright, so the next mutation or fusion that we're going to talk about is RET fusions in lung cancer. They are bona fide, lung cancer drivers with an incidence of 1-2% in the non-squamous, non-small cell lung cancer population. Usually exclusive with other driver mutations. Up to half of patients with advanced disease have brain metastasis. Most frequent kinase C family member, or which one on the Exon is that 5KIF-5c, REC primary protein, juxtaposes, KIF-5b, Exon-15 and REC Exon-20.Other common fusions are listed there. Many other fusion partners have also been identified. So, the two drugs of FDA approval is selpercatinib and pralsetinib. And then, when we looked at these, both of them were approved in 2020. When we looked at some of the data from these trials, we have a phase 1 and 2 trial for both of them, selpercatinib and pralsetinib. When we look at the overall response rate in that prior platinum-based chemotherapy patient it's 51%, at treatment-naïve it's 84. Obviously you've got more of a robust response there. When we look at the pralsetinib, in that prior treatment overall response rate was 59%, and 72% in that treatment-naïve in – with it, as well as the median DOR and the median PFS.

So, when we look at the dosing and side effects, when we look at selpercatinib, it is weight dosed. It's general, but it's still weight dosed, and it is a twice-a-day medication, and the pralsetinib is a daily dosing. Common side effects, you're looking at, in terms of selpercatinib – dry mouth, diarrhea, hypertension, fatigue, constipation, nausea, abdominal pain, edema, rash and headache.

Pralsetinib has a less profile in terms of common side effects, which is fatigue, constipation, musculoskeletal pain, but still get hypertension. And then grade 3 side effects happened rare, equal to 2%, are listed there. I will bring to your attention that hypertension – that is really something that you just want to make sure you educate the patient on well about. Monitoring for, and managing, hepatoxicity associated with RET-specific inhibitors, as I said, the hypertension, you just want to make sure that you're optimize it, the blood pressure, before starting drugs, monitor blood pressure during, after one week, and then monthly. And however you are going to correspond that – is that going to be your EMR system or a phone call? Grade 3 if you're withholding, it persists, despite optimal antihypertensive therapy, and I would say, even make sure that their blood pressure – oh, I see it there, optimize the blood pressure before starting. This – I can't stress that enough. Don't start patients on this drug without knowing what their baseline, what their trend is.

Hepatoxicity – we're doing those labs. Still doing a CBC and a CMP. You're going to monitor those ASP and ALT prior to, every 2 weeks, and first 3 months. And if you have the luxury of having a oral chemo pharmacist or if there's pharmacists on this virtual program, they're so key, especially with all these oral therapies. So don't feel – you know, I've utilized ours on a regular basis, so just make – you know, because there's a lot of TKIs, especially with lung space, especially if you don't do it day in and day out, you need to utilize your pharmacist if you have one available.

Hemorrhagic events – advise patients about risks of bleeding, with drug, and to contact. There's no cure provided. Any sign or symptom of bleeding – and you list those – those modifications that are in that last column there.

So when we look at end-TRK rearrangements and TRK views in the cancer, normal, well and neural, development in utero, and post-nasal neural differentiation, they can go, not just – they're not exclusively to lung cancer, and that's what this slide here is telling us.

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When we look at the TRK inhibitors, we're looking at the drug entrectinib and larotrectinib. For the sake of time, I'm just going to try to kind of hit on some key percentage data that have come out of this study. When we look at the overall response rate was 83.6 in the entrectinib arm. Median overall survival had not been estimate. The median follow-up was 19.2. When we looked at the larotrectinib arm study, the overall response rate was 73%, and the median overall survival was 40.7.

So, let's move to the HER2 mutations in advanced non-small cell lung cancer. This is our new one to the mix. This was approved back in 2022. The incidence is 2-3% of non-squamous, non-small cell lung cancer.

HER2, or you may see it on your report as ERBB2 mutations, is different from HER2 overexpression or HER2 amplification. There is potentially a higher propensity for brain metastasis while on treatment for patients with HER2 mutations versus those with KRAF or EGFR mutations. In the TDS-B, HER2 positive, ADC coupling, and an anti-HER2 MAD, or monoclonal antibodies with trastuzumab, sequenced to a particular inhibitor payload using a tumor select depletable linker. So, in – simply stated, think of it like a ball. On the outside is the trastuzumab and the inside is this targeted therapy. It goes to the cell, it opens up and that's how it kills the cancer cell.

This was based off of the phase 3 DESTINY LUNG-02 trial, where looked at trastuzumab deruxtecan in pretreated, HER2 mutated, metastatic patients. So this, again, second-line therapy. Again for the sake of time, I'm just going to try to hit some of the key points on this slide. One thing you need to know that both prior or platinum showed a response rate, and that the efficacy outcomes, the median DOR endpoint was 8.7, to confirm overall response rate was 57.3. Some of that, just to touch on it, any grade there was 92.1% of AEs. When you looked at grade 3 or higher, it was 31.7, and so just kind of keep an eye on this drug, in terms of associated with drug discontinuation, reduction, interruption and what there – the ILD percentage was as well.

So, patient-specific molecular profile determines treatment course. Choose therapy directed toward each patient's specific non-small cell lung cancer genotype, as determined by BRAF molecular profiling, preferably NGS. Most CKRs are now recommended as first line therapy for patients with the specific pr and mutation. For many patients diagnosed with advanced non-small cell lung cancer, the best therapeutic options may be a clinical trial. Patient specific molecular profile determines deterioration. It's that Chose therapy. As I said, the action item is to select therapy based on a result from molecular profiling, and the evidence from clinical trials.

So, let's kind of switch the gears. I know we're kind of rushing on time, but I'm going to try to get this in, and still have some time for questions. We're going to now move to potential lack of efficacy with immune checkpoint inhibition and EGFR mutation positive, non-small cell lung cancer. In a nutshell, what this trial shows us is that when you are starting a patient on a immunal therapy __ with the EGFR mutation, you really have a lesser response rate than if you would have started that patient on their target therapy up front. Potential toxicity with sequential use of immunotherapy, followed by TKI – another reason why you need to know that, that mutation, retrospective review of patients' records to identify severe toxicity with ICI and EGF TTR, regardless of sequence in patients with EGFR mutations.

In patients treated with osimertinib within 3 months of an ICI, there was 24% enveloped a severe IRAD. Conversely, there was none if you went the other way – if they started on a target therapy, EGFR mutation, and then went to, on immunotherapy or ICI.

High PD-L1 expression does not exclude the presence of a targeted mutation, so you may have again, they need NGS testing, so please test them, not just PD-L1. Efficacy to immunotherapy potentially reduced in patients with a driver mutation. Giving immunotherapy up front in a patient who has a driver mutation may increase the risk of AEs with prior therapy later. So again, review molecular testing results before initiating treatment in patients with advance non-small cell lung cancer, even if that PD-L1 comes back high because remember, PD-L1 comes back very quickly.

So, immunotherapy. This is the landscape of 2023, as it relates to immunotherapy in advanced non-small cell lung cancer, without an actionable mutation. As you can see, the list is long, and when we look at some specific updates as it relates to immunotherapy, this is the phase 3 adjuvant immunotherapy trial, where it looked at adjuvant of immunotherapy, post-resection, post if they got the chemotherapy. So the primary endpoint was EFS by investigator, and this trial looked at pembrolizumab versus a placebo. Again, patients with stage 1B, post-surgical resection, no mutation identified. So when we looked at this, the DFS in overall population for ICC. Here is the – both of the graphs, we looked at the median DFS. In the EMPOWER-010, you see that atezolizumab arm had not been estimated, and when we looked at the PEARLS and KEYNOTE, when we looked at pembro versus placebo, the median DFS was 53.6 versus 42.0.

Phase 3 CHECKMATE 816 neoadjuvant, so this is getting immunotherapy even prior to resection, plus the chemotherapy for stage 1B-3A in non-small cell lung cancer. The EFS over 3-year update, when you looked at nivolumab plus chemotherapy, in those patients the median EFS had not – was not reached. When you looked at chemotherapy alone, it was only 21.1 months.

So, in immunotherapy for early stage non-small cell lung cancer summary, adjuvant therapy approval. Atezolizumab – that is approved based on the EMPOWER 010, adjuvant treatment following resection, plus platinum-based chemo in stage 2-3A non-small cell lung

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cancer, with tumor PD-L1 expressions of greater than or equal to 1%. Pembrolizumab was based on the PEARLS study. Adjuvant treatment following resection, plus platinum-based chemo, in stage 1B or stage 3A, non-small cell lung cancer, regardless of PD-L1 expression. The overall survival data is immature for both.

In the neoadjuvant therapy approval, the only approved one, as of now, is nivolumab, which is based on the CHECKMATE 816. Neoadjuvant treatment in combination with platinum-based chemo in resectable non-small cell lung cancer.

Summary, when to test: at initial diagnosis, locally advanced disease, at disease progression and at disease recurrence. I can't take the – you cannot leave without understanding that. These are the times when patients need to be tested. And now that there are target therapies and immunotherapies that are available, again in that early stage, that initial diagnosis, disease progression, and at disease recurrence in the local readvancement. So, our action plan: order biomarker testing, preferably NGS, to identify actionable mutations in all patients with advanced, non-squamous, non-small cell lung cancer, and consider in those patients with squamous non-small cell lung cancer. Proactive mitigation and management of diarrhea associated with mobocertinib, in patients with EGFR Exon-20 insertion positive in advanced non-small cell lung cancer may reduce the severity. Proactive mitigation and management of edema associated with selected met inhibitor therapy in patients who harbor the met Exon-14 may reduce its severity. Select therapy based on the results of molecular profiling and the evidence from the clinical trials. Remember to wait for that complete, complete molecular test and results, before initiating treatment in patients with advanced non-small cell lung cancer, even when their PD-L1 IHC results show high aggression.

Dr. Sims:
So, we have a question. Are you suggesting that platinum-based chemotherapy is better than other chemotherapies, to penetrate CNS?

Ms. Persinger:
No, not at all. What we do know is that chemotherapy does not penetrate the CNS well at all. Our best options are some of these TKIs, especially with osimertinib. We know that it has a great CNS penetration, and so sometimes you will see in – well, in our clinic, we will get a patient that may progress while on osimertinib, but if they still do not have any brain metastasis, we will continue them on osimertinib and start that chemotherapy. So no, I am not suggesting that there are certain chemotherapies that penetrate better into the CNS space. We don't have that answer.

Dr. Sims:
Right. I want to thank you for sharing. This has been a great talk. I've learned a lot today, actually, and certainly, a good understanding of the need for biomarker testing and NGS testing. So, thank you so much for educating all of us today. It's a great presentation, and I want to…

Ms. Persinger:
Thank you for having me.

Dr. Sims:
…thank you for it, and the audience. We'll see you at the next presentation. Thanks again.

Ms. Persinger:
Thank you.

Announcer Close:
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