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Keeping Pace in Lung Cancer – How Would You Treat? Case-Based Learning in EGFR-Mutant NSCLC

Announcer:
Welcome to CME on ReachMD. This activity, entitled “Keeping Pace in Lung Cancer – How Would You Treat? Case-Based Learning in EGFR-Mutant NSCLC” is provided by Prova Education.

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Dr. Socinski:
Welcome to the Keeping Pace in Lung Cancer educational series. With the ever-evolving genomic landscape in non-small cell lung cancer, it is imperative to incorporate molecular profiling into the diagnostic journey. Let’s dive right into EGFR-mutant non-small cell lung cancer. This is CME on ReachMD, and I’m Dr. Mark Socinski.

Dr. Heymach:
And I’m Dr. John Heymach.

Dr. Socinski:
So let’s get started. EGFR mutations are the most common genomic variant in non-small cell lung cancer, and there are a vast number of treatment options available. With the complexity of EGFR-mutant non-small cell lung cancer, treatment selection and sequencing admittedly is an art. To demonstrate this, we’ll walk through a patient case together. We’ll consider diagnostics, appropriate sequencing of available therapeutic treatment options, and what to do when a patient progresses on a frontline agent. Dr. Heymach, do you have a case for us?

Dr. Heymach:
Sure. I can take you through a patient I’ve been following now for a little bit more than 2 years. So the patient is a 58-year-old, nonsmoking, woman from South Texas. That’s relevant because Texas is a very big state; she lives over 300 miles away, but people will drive long distances here. And she presented with a persistent cough. She had been to a primary doctor several times and gotten antibiotics, had been treated, it got a little bit better then it recurred, was treated again with antibiotics. During this time, she had worsening back pain, and eventually, as part of a workup for back pain, an MRI was done, and it showed suspicious lesions on her back, and that triggered a workup that saw a right upper lung mass, some mediastinal adenopathy, and a PET scan showed several presumed bone metastases, 3 or 4 of them as I recall. We ended up sending a liquid biopsy test in addition to ordering a tissue biopsy. Initially the tissue biopsy did not have sufficient tissue. The liquid biopsy revealed an EGFR L858R mutation, so a classic, exon 21 mutation. That was her initial presentation.

So let me pause there. Dr. Socinski, do you want to take us through your initial thoughts about this and, you know, how you would handle the diagnosis of patients like this, molecular profiling, and so forth?

Dr. Socinski:
Yeah, this is a clinical presentation that we see not too infrequently, actually, never-smoker who presents with stage 4 disease. The biopsy presumably showed adenocarcinoma in this patient; she’s a never-smoker, as you mentioned. There are always issues with the

adequacy of the initial tissue biopsy, and certainly plasma-based testing is a very clinically useful approach in doing comprehensive genomic testing. You know, I think in these patients the critical aspect is to do it – in my clinic, I actually test both the tissue as well as plasma on a next-generation sequencing platform to make sure that we cover all of the potential genomic alterations that are out there nowadays. Remember we have 9 biomarkers in which the FDA has approved targeted therapies for. So it's important that that initial comprehensive testing does cover all of these targets because of the availability of treatments, generally which tend to be more effective, at least from a response rate point of view, than standard chemotherapy. And in general, this is a population that doesn't enjoy as much benefit from immunotherapy as, say, a smoking population might. So the concept of comprehensive genomic testing is important. In this case, you found probably the most likely thing, which was an EGFR mutation. We know the vast majority of the EGFR mutations are either the exon 19 deletions or, in this case, the exon 21 L858R mutation. I think from a therapeutic point of view, she obviously is symptomatic from stage 4 disease. I think the 2 options that one might consider, would be osimertinib based on the FLAURA data. It showed it was superior to first-generation drugs in this setting, both erlotinib and gefitinib. With slightly better toxicity profile also, and there's also the ease of the convenience of taking a once-a-day pill.

You know, we've had some interesting data recently with regard to the use of erlotinib plus ramucirumab, particularly in the exon 21 L858R population, showing activity very similar to Osimertinib, also, but obviously a very different approach. A first-generation EGFR TKI in combination with an anti-VEGF drug.

So, John, you've always had an interest in targeting VEGF, and this is a population which may get greater benefit from targeting VEGF. I wonder what your thoughts are, and what did you do in this particular case?

Dr. Heymach:
Yeah, well, we presented exactly those opportunities to her. So on one hand, there's osimertinib, as you mentioned, well-tolerated, active drug. But we also discussed with her the RELAY regimen, so the combination of erlotinib and ramucirumab. We went through the pluses and minuses here. You know, the fact that she had an EGFR L858R mutation, that's a mutation that tends to not do as well with osimertinib as the exon 19 deletion. It seems like from the RELAY regimen that L858R-mutation patients did not have that detriment that they did with osimertinib. So sometimes with the L858R mutation, that'll push people towards the RELAY regimen. As you mentioned before, osimertinib is well tolerated and oral. In her case, you know, as I went through these different options, she found it very appealing that she could potentially get osimertinib after the RELAY regimen if she had a T790M mutation.

Dr. Socinski:
So, John, tell me, have you had experience with the RELAY regimen, the erlotinib plus ramucirumab?

Dr. Heymach:
This is a regimen that I do discuss with patients who are newly diagnosed, those who don't have brain metastases, and particularly for those with L858R mutations; those are a bit tougher to treat. And what I discuss with patients, the combination of ramucirumab and erlotinib has virtually identical outcome as osimertinib in the first-line setting but has the option that if resistance developed by a T790M mutation, patients can then go on to osimertinib in the second-line setting if they do have that mutation. So essentially it gives patients the possibility of avoiding chemotherapy for longer.

So I review this with patients, and I have used it a number of times. I think it tends to be patients that have a better performance status, don't have brain metastases, and in my experience, patients who are willing to come in for the treatment every few weeks and are more interested in retaining as many options as possible as they go along. So in this case, I think this is absolutely an appropriate regimen because you have similar outcomes in the first-line setting but retain the possibility of using osimertinib later.

Dr. Socinski:
And I think it's important to note that on the RELAY trial, the rate of the development of T790M was the same whether or not the patients received ramucirumab.

Dr. Heymach:
So that was certainly a plus. And that's just one of the reasons why it really seems worthwhile to profile your patients on resistance. Have you, Dr. Socinski, come across other mechanisms of resistance you've been able to target after biopsying these patients?

Dr. Socinski:
I think the concept of re-biopsy is important. In a case like this, it was very informative. And here you have substantial clinical benefit from what you learned with the process of retesting, whether it's a tissue biopsy or whether it's a plasma-based next-generation sequencing approach. So, you know, there've been reports of other secondary EGFR mutations, not quite clear how to handle that. There've been other bypass tracks that have been described that may offer an opportunity for a targeted approach. So I think the take-home message here is to think about retesting patients at the time of disease progression because you may open up a very good option

for them that you otherwise wouldn't know about or think about if you didn't do the testing.

Well John, this has been a fascinating conversation. Before we wrap up, I just gave my take-home message about retesting and how it can be helpful, in certain cases, to direct therapy. What's your take-home message for the audience today?

Dr. Heymach:
Well, first of all, that treatment options for EGFR-mutant patients is really growing rapidly; we've got a couple good first-line options now. Osimertinib, the RELAY regimen with ramucirumab and erlotinib are both good options. New options are coming. And there's a lot of these resistance mechanisms that are targetable. I agree fully with you that it's important to biopsy these patients at progression, understand why the resistance is happening, and then either look for an appropriate combination or look for a clinical trial, where appropriate. And we always have chemotherapy down the road. Fortunately we haven't had to go to chemotherapy yet for my patient here from South Texas, but we do know that is an option down the road if needed.

Dr. Socinski:
Always an option.

Unfortunately, that's all the time we have today. So I want to thank our audience for listening in and thank you, Dr. Heymach, for joining me and sharing all your valuable insights. It was great speaking with you today.

Dr. Heymach:
Yep, thank you as well.

Announcer:
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