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Keeping Pace in Lung Cancer: Clinical Case Challenges in NSCLC

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Dr. Socinski:
Hello, and welcome to this lung cancer activity, which is part of the Keeping Pace in Lung Cancer series. This is CME on ReachMD, and I’m Dr. Mark Socinski.

Dr. Levy:
And I’m Dr. Benjamin Levy.

Dr. Socinski:
So let’s get started, Ben. We’ve now incorporated immunotherapy into the treatment algorithm for non-small cell lung cancer. This has given us an additional layer of complexity when selecting the appropriate treatment option in the first-line setting. So let’s try to untangle some of the data. I’ll let you walk us through the first case.

Dr. Levy:
Thanks Mark. I hope this case can underscore and highlight some of the challenges that we have with therapy selection in the treatment-naïve setting for patients with advanced lung cancer. So this is a 71-year-old female. She’s a former smoker, has a 40 pack-year history. She quit 1 year prior to the presentation. Her past medical history is only significant for hypertension, and she presented in 2018 complaining of a worsening cough, chest heaviness, and exertional dyspnea. Her primary care physician ordered a chest X-ray that was followed by a CT scan, and that CT scan unfortunately revealed bilateral lung nodules. She went on to have a CT-guided biopsy that demonstrated or was consistent with a TTF-1 positive adenocarcinoma. Importantly, her PD-L1 was 60% and her genetic interrogation did not reveal any actionable mutation outside of a KRAS STK11 mutation. She had full staging with both a PET scan and a brain MRI, and her MRI of the brain was negative, but the PET scan did unfortunately show bony lesions as well as liver lesions. So the patient came to me for a discussion of therapy selection.

So, Dr. Socinski, how would you approach selecting the appropriate optimal first-line treatment for a patient like this?

Dr. Socinski:
Well, in a patient with greater than 50% PD-L1 expression, it opens up the option of immuno-monotherapy. We know we have 3 options. Pembrolizumab was the first, atezolizumab the second, and now cemiplimab, most recently, all have data compared to platinum-based chemotherapy that they are superior in this subset of patients. And there’s also a suggestion from the cemiplimab trial that the higher the PD-L1 expression, the greater the benefit is relative to platinum-based chemotherapy. Those patients with 90% to 100% PD-L1 expression versus those with 50% to 60%.

In these patients, if they are relatively asymptomatic or minimally symptomatic and don't have an overwhelming tumor burden, I think immuno-monotherapy is typically my choice. It does offer superior response rates. It does offer a better overall survival and tolerability for these patients. So it's a very attractive option in these greater than 50%. I have evolved into thinking that the higher the PD-L1 expression is the more likely I am to use immuno-monotherapy. But, Ben, you and I both know that there are patients in this subset of greater than 50% that may not be best served by immuno-monotherapy. Your comments on this?

Dr. Levy:
Such an important point because I think treatment selections are nuanced here and not only have to factor in the PD-L1 but have to look at patients' symptom burden, potential performance status, on whether or not single-agent immunotherapy is going to be the optimal regimen. The higher the PD-L1 expression, the more likely they are to respond to immunotherapy. PD-L1 is a continuous variable.

That said, I think there are patients in which we need to consider combination strategies. So for a patient with heavy disease burden, patients who are reasonably fit, and patients who are symptomatic, that would be, I think, an opportunity to consider combination strategies in the greater than 50%. What are those combination strategies? Well, clearly chemo/IO is one, and KEYNOTE-189 certainly is an option for patients like this with a PD-L1 greater than 50 who may have heavy disease burden, so carboplatin/pemetrexed/pembrolizumab. We've got new regimens. We've got CheckMate 227, which is a dual checkpoint blockade with nivolumab plus ipilimumab. We've got CheckMate 9LA which is nivolumab plus ipilimumab plus 2 cycles of platinum chemotherapy. We have the IMpower150 regimen with carboplatin/paclitaxel/bevacizumab/atezolizumab. That may also be a potential option. We've got subset analysis from that dataset suggesting patients with liver mets may do well. So I think all of these options are reasonable. Certainly, a shared decision needs to happen with the patient on this because the greater than 50%, yes, you can use single-agent IO, but we also have combination approaches that we can also use, and that can sometimes be a nuanced treatment decision that needs to sometimes involve the patient.

Dr. Socinski:
I would agree. So let's transition. Again, as we've mentioned, it's only a minority of patients that have high PD-L1 expression. What about those patients that are in the 1% to 49%? Do you have a second case to discuss?

Dr. Levy:
I agree. I think the greater than 50, we've got a lot of options. We certainly have a lot of options in the less than 50 or the 1 to 49. So this is a 58-year-old male. He's a current smoker. He's got a 30 pack-year history, but he quit upon the diagnosis of his lung cancer. He's a relatively healthy guy. He has no real comorbidities, and he's been newly diagnosed with stage 4 lung cancer with brain metastases. He has a biopsy and the PD-L1 expression is 10%, and his genetic interrogation is unrevealing for any actionable mutations. So we have a patient who's relatively fit with brain mets; PD-L1 is 10%. Mark, how do you talk about treatment selections for these patients?

Dr. Socinski:
We just had a very nice discussion about the greater than 50%. The major difference to me in the 1% to 49% is that knocks out, in my opinion, any option for immuno-monotherapy. We had a very nice presentation of an FDA analysis of looking at this 1% to 49% comparing immuno-monotherapy with chemo/IO strategies, and clearly immuno-monotherapy was inferior to the use of chemo plus IO specifically in this population. Other than that, Ben, I think the discussion that you had before with regard to the multiple options apply to this patient, also. Your thoughts?

Dr. Levy:
Yeah. I think, again, competing strategies here. Treatment decisions need to be nuanced. We've got a lot of options on the table. We've got KEYNOTE-189 with carbo/pem/pembrolizumab. We've got CheckMate 227 with nivo/ipi. We've got, you know, CheckMate 9LA. As you mentioned, Mark, IMpower150, for bev-eligible patients, is an option. We've got, atezo plus carboplatin nab-paclitaxel that's approved. So we've got a lot of different options. I can say for most of my patients with adenocarcinoma, as I mentioned in the last case, I tend to use carboplatin/pemetrexed/pembrolizumab, but I am starting to look at the dual checkpoint blockade, how it's used, how it's leveraged, either alone or in combination with platinum doublet. And I would say, again, for those patients with liver mets who are bev-eligible, I think the IMpower150 regimen is certainly one to consider. So it's getting complicated out there. That's good for patients, and the more options we have, this generates a lot of confusion, but that confusion translates into better outcomes for our patients.

Dr. Socinski:
Yeah, I would agree. It allows you, to a certain extent, to tailor treatment once you nuance the patient. One of the frustrating things is the progression of disease. This is a challenging situation both for us as well as the patient. What are your thoughts about transitioning to second-line therapy after, say, chemo/IO in the first-line setting?

Dr. Levy:
Yeah, I think this is one of the more difficult scenarios we face in our clinic every day. I mean we have all of these great frontline options.

The question is if and when there's disease progression, what do we do? I think, importantly, we have to have a case for clinical trials in this space. And there's just a lot of clinical trials out there, and, yes, it's like throwing spaghetti on a wall and seeing what sticks. Some of these trials look promising, some of them don't, but we try to screen patients for clinical trials given the lack of evidence we have as to what to do in this setting.

Now, I would say for patients off of trial, I tend to default to a taxane, and if patients have no contraindications, I will consider adding ramucirumab to docetaxel. And there may need to be some dose modifications to that as it relates to not only the dose but the schedule of how to deliver it. But that would be my default chemotherapy based on the REVEL trial. Although the REVEL trial did not allow prior chemo/IO, this was done before chemo/IO was first line. I think there are other options. Medicine as an art, not a science. But certainly, gemcitabine is an option, too, for those patients who may have neuropathies or can't tolerate docetaxel ramucirumab.

I'll tell you what I don't do, which I think is also important, which is that I don't sequence to another immunotherapy. If patients are receiving platinum pemetrexed with pembrolizumab and have disease progression, I'm not moving on to atezolizumab; I'm not moving on to dual checkpoint blockade. I see that being done; I just don't think we have a lot of data there. But a very difficult space right now in terms of what we should do for these patients.

Dr. Socinski:
I agree. One of the things that I wanted to also get your thoughts on is, with these types of immune treatments, there's certainly a potential for immune-mediated adverse event. This is a spectrum of toxicity that we don't see with other classes of drugs. How do you proactively manage these immune-related adverse events in your day-to-day practice?

Dr. Levy:
I manage them carefully. A call for interacting and engaging with our subspecialists. It's a call for looking up how to grade these. I'll tell you, even as a lung cancer expert and somebody who gives immunotherapy in my clinics almost every week, we always want to grade these appropriately so we know how to manage them. I think there are a lot of different resources that can provide support on grading these immune-related adverse events. And then managing them appropriately. And I think we could go on and on about all the different immune-related adverse events. But I think, importantly, we need to grade them; we need to engage our subspecialists to help us. And then of course, when we're talking about things like instituting steroids or holding therapy, a lot will depend on grading them and partnerships with our subspecialists. And that's part of the proactive management that we have.

Dr. Socinski, any additional insights into how you approach these at a high level or even day to day?

Dr. Socinski:
I would offer similar comments. I think it's imperative that all oncologists, including oncology nurses, understand that this is a wide spectrum. Pretty much any part of the body is at risk of an immune-related adverse event, and very weird and uncommon, rare things have occurred like myocarditis, type 1 diabetes, so on and so forth. You have to be vigilant. They typically occur early, but they can occur at any point in the management of the patient, sometimes even after discontinuation of the drug. It is something that really needs vigilant attention over time. But I would echo your comments, also.

So, Ben, this has been a fascinating conversation. Before we wrap it up, can you share one of your take-home messages for the audience?

Dr. Levy:
Don't be afraid to engage resources to help guide you on this, whether it be NCCN guidelines, whether it be subspecialists to help with management of adverse events, whether it be reaching out to an expert. The world in lung cancer has gotten exceptionally complicated and nuanced, and we certainly, even as experts, sometimes struggle with what to do, and it takes a village. I would say at a very high level, not hesitating to reach out to those resources or supports to help guide you in the management, given all the competing strategies that we have. And once again, this complexity is coupled with enthusiasm that in turn has led to better patient outcomes. But we're all in this together, so I would just make that point as we move forward.

Dr. Socinski:
I completely agree.

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

Dr. Levy:
Thank you, Dr. Socinski.

Announcer:

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