Case Based
Panel Discussions
Lung Cancer 2018

Choosing between Targeted Therapy and Immunotherapy in a Patient with an EGFR Mutation and High PD-L1 Expression

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TRANSCRIPT

Dr. West: If you turn on the television you're likely to see TV ads about immunotherapy, often for lung cancer, and there's a couple Opdivo, Keytruda out there. There's others that are studied, but not as much on TV, but just as likely to be in the news. And of course we have many patients who come in asking for these, including perhaps some patients who may be better suited for other approaches.

One situation that we see is patients who have a driver mutation, like an EGFR mutation; it's about 10% of our patients. It's more likely in never smokers or people who have a minimal smoking history and an adenocarcinoma. I see a lot of these patients. I know that you do as well, Zosia. So, I've had patients who we recommend an oral targeted therapy against this that can work very well, but the patients are interested in the immunotherapy. They've seen on the news or read about and are really excited about that instead of the pill-based therapy.

One point to make is that these patients who have a known EGFR mutation have been excluded from the first line trials. Importantly, my understanding of that is a) because we have a very, very good alternative approach that we can't be confident that the immunotherapy approaches are going to be better than; and second, we haven't been that confident that immunotherapies work that well in these patients, based on at least the trials that gave these immunotherapies a second or third treatments. The patients with EGFR mutations have generally not done that well.

But let's take a patient who comes in and has high PD-L1. This is about a third of our patients, and so it is certainly very possible that someone will have an EGFR mutation that would suggest a pill to target that could be very good. But on the other hand they have this high PD-L1, a protein that is predictive of a good response to immunotherapy. So there could be a couple of

options to think about, that the patient and/or their oncologist would be considering. What would you say is the optimal approach here? Let me start with you, Taofeek.

Dr. Owonikoko: I think what we are learning now is that while immunotherapy is very good, is very helpful for a sub-set of our patients, it is not for all patients.

Dr. West: At least as a first treatment.

Dr. Owonikoko: At least as the first treatment. It is not a good option for all patients as the first treatment to go through. And one of the sub-set of patients where that is particularly important to establish is for those patients with driver mutations like EGFR mutation or ALK because 1) the studies that led to the approval of these drugs, that assured us that they are very good, excluded most of these patients, so they did not contribute to that data set.

But more importantly now is, as we are now beginning to see emergent data, now data that is newly generated in patient, not going back to look at old data to see how people behaved. So a small study that was presented at the recent ASCO meeting, looking at only about 10 to 12 patients with EGFR mutated lung cancer and with very high PD-L1. So the biomarker was very high. So, yes, these are patients who are likely to benefit from immunotherapy. Actually, it turns out that when you treat those patients with Keytruda first rather than the targeted therapy pill, whether it was osimertinib or Afatinib or any of the other pills, the outcome was very, very poor. They did not derive as much benefits, and even those that had some response, it did not last. And more importantly, once they progress on the immunotherapy drug, it became a real challenge to put them on the oral pill, suggesting that we might actually be compromising the established benefit of the pills, the targeted pills, when we treat these patients first with immunotherapy.

So my take home message from that data set that we have, granted it's a small data set, but at least it reinforces our practice pattern now, which is for patients with driver mutation the best thing to do for them, as first line treatment, is targeted therapy and then after that we can consider other options.

Dr. Piotrowska: I completely agree. I mean, I think the great thing for these patients is that we do have very, very effective therapies that not only work well but also are very well tolerated. These are often pill therapies; patients are able to really continue their normal lives, often just coming to see us once a month, once even every few months. And they can work very well for a long time. So we have a great option.

But we also know that for these patients, whether you look at newly diagnosed patients like with the data from ASCO this year, or in later lines of therapy, immunotherapy, despite all its hype, it just doesn't seem to work as well for these patients. And I think this data that came out of ASCO this year is very important because often the way that testing comes back, PD-L1 comes back much, much faster than the molecular testing, than the EGFR testing or ALK or ROS-1. And so there's a temptation when you see that positive PD-L1 testing to say, "Okay, great. Let's go – immunotherapy is the right treatment for you." But I think for patients where, you know, particularly among never smokers or patients where we think the likelihood of a mutation is high, and really I think for any patient, it's worthwhile waiting for that molecular testing because

you really want to have all of the information at hand. you want to understand what type of cancer is this, what is really the best therapy for this patient before starting that treatment. Especially in a situation where you can sometimes see that if you start the wrong treatment you can actually have a detriment, not only for that treatment but for later their ability to tolerate the treatment that they really need. So I think for that reason it's important to get all of the testing back, not just PD-L1 but also the molecular testing to be able to select the best therapy.

Dr. West: I think this was, even though it was a small study and it wasn't the most featured study, it has pretty significant clinical implications to us. The fact that it was a small study, it had a very big effect, and it closed early because the investigators were so concerned about the poor outcomes of these patients. There were two patients with an EGFR mutation who had died in the first six months, which is really quite unusual, and the fact that one died of side effects of inflammation in their lungs (pneumonitis) while on Tarceva, which we rarely see, after being on immunotherapy raises the concern that guessing wrong can have real consequences.

I think you make a great point as well that you can't just say, "Okay, I've got my PD-L1 test; I can give Keytruda, let's go," unless you've checked the other things to make sure that the others are negative because you could really do a patient harm in the setting of having one of these driver mutations, this would be a wrong choice, Keytruda would.

And so, overall, I think we're at least speaking with one voice that this just reinforces that a targeted therapy is the right treatment, even in patients who have high PD-L1 and that if you're going to consider immunotherapy it's not to say never, but you would really want to defer that until after you've gotten the benefit you can get from the therapies targeting that driver.

END OF RECORDING