Case Based
Panel Discussions
Lung Cancer 2018

# Rapidly Progressing Lung Adenocarcinoma and High Tumor PD-L1 Expression: How Would You Treat?

**Presented by Drs Zofia (Zosia) Piotrowska, H. Jack West, and Taofeek Owonikoko**

## TRANSCRIPT

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**Dr. West:** We sometimes see patients we can tell have a rapidly progressing cancer. This is information that we might get from them coming in feeling much worse than they were a month ago, losing a lot of weight in the last few weeks. They might have had an initial CAT scan in the emergency room a few weeks ago and then had a PET scan just in the last few days before you finished your work up and it shows marked change just over two or three weeks. And so we have an indication in some patients that they have much more aggressive disease, they have a large burden of cancer, and they're sicker. And yet they still might be fit enough to think about whatever we might want to do for them.

Let's take a patient who has an adenocarcinoma, a non-small cell lung cancer metastatic disease, and no driver mutation. No EGFR and no ALK. And we've tested for PD-L1, the marker, the protein on some cancer cells, and if there's a high level of expression, it is associated with a better chance of responding well. In this particular patient, the PD-L1 level is 60%. And so that's in the range where we would be able to give immunotherapy, Pembrolizumab or Keytruda, as a single drug. We've got evidence from a couple of trials now that, compared to chemotherapy alone, Keytruda as a single drug does well. But we also have evidence from another trial called Keynote-189 that gave chemo with or without immunotherapy (again, Keytruda in this case, the chemo being Cisplatin or Carboplatin with Alimta) that suggested that the outcomes were very favorable for the patients that got chemo with Keytruda compared to chemo alone. So, both Keytruda or chemo and Keytruda are better than chemo alone, and they're both FDA-approved options.

How do you approach this patient and what you think is going to be the best treatment for somebody who is losing weight, is sicker, but is still a candidate for everything you might consider for them? Taofeek?

https://www.youtube.com/watch?v=TC_mKK04QQs&feature=youtu.be

**Dr. Owonikoko:** For a patient like this where you have heavy disease burden and a lot of symptoms, so really what you want to do is arrest that process as quickly as you can. But we have to differentiate between two things: one is symptoms due to the disease and then symptoms due to other problems that the patient might have. So if all of what we're looking at is primarily from the disease itself, and there is no other contraindication, we know that this is a patient, from what you've described, with high biomarker. So whether you use single-agent Pembrolizumab or Keytruda or the combination with chemotherapy, they're likely to do very well.

But we also know that immunotherapy tends to work better when you don't have a lot of disease. So in that situation my inclination would be to use the combination of chemotherapy and immunotherapy together, provided the patient can tolerate it. If the patient is really declining very, very quickly and I'm afraid that layering chemotherapy on top of immunotherapy might cause us more harm in the short term than good, then if you actually look at the data, for those with high PD-L1 expression, the time to the patient responding is about 2.2 months, which is similar to the time to the patient responding from the chemotherapy and immunotherapy combination regimen. So, you actually may not be able to induce response any sooner by giving chemotherapy. The only thing is it might be able to induce deeper responses when you add the chemotherapy to the immunotherapy.

So, if I think the patient is too frail, primarily from the disease, and they have high biomarker, I might go ahead with single-agent Keytruda in this instance, because a newly diagnosed patient and that is the only approved agent that we can use in that setting. Arrest that process and then, once the patient is stronger, then we can reassess where we are and consider whether adding chemotherapy or just continue.

**Dr. West:** We could presume that this patient is probably still fit enough for treatment, for any treatment, but still with the indicators that this is going to be an aggressive, difficult cancer. Zosia, what's your approach here?

**Dr. Piotrowska:** Yeah, I agree. I think that either approach would be very reasonable. Either approach has a good chance of success for a patient like this. And I think one thing to say, you know, for someone like this we really try to get this treatment started as quickly as possible, and that's important. And this is someone where I might bring them back within just a few days of meeting them to start treatment, sometimes even in the hospital if they're sick enough. But I do think that if you look at the response rates, the chances of the actual tumor shrinking in the different studies, in the Keynote-024 study where high PD-L1 patients were given Keytruda alone, the response rates for the high PD-L1 patients, I believe around the 40% range—

**Dr. West:** 45%.

**Dr. Piotrowska:** 45% range. Whereas in Keynote-189, which combined chemotherapy together with Keytruda, the response rate, the chances of the tumor actually shrinking, were a little bit higher, in the 60% range. These are two different studies. You can actually take those numbers and compare them head-to-head, but nevertheless it gives you a sense that the chances of actually shrinking the tumor and arresting that process, as you say, Taofeek, are a little bit higher if

you're able to give the chemotherapy and the immunotherapy together. So for a patient that I think can handle it, that would be my preferred approach.

**Dr. West:** I would say I agree that, of course you're going to need to say whether this patient can really tolerate it, but I would be inclined to favor the combination in a patient like this for a couple of reasons. One, 45% response rate is quite good by historical numbers, but if your alternative is more in the range of 60% or higher, then you're going to want that, particularly in patients where you'd like to see that response as soon as possible. And I think, yeah, there's not a big difference in the time to response if people are going to respond. But to me, also, the bigger issue is if this is a fast-growing process, you run the risk of a patient declining quickly if they aren't in the fortunate proportion (if they aren't in that 45% or 60%). These are drugs that work somewhat different and I would like to make sure that they get their opportunity with both chemotherapy and with immunotherapy.

So, if they're strong enough to get it, the only way to be sure they'll get both is to give them concurrently. I think of it like getting two shots on goal; I'm not as confident I'm going to be able to deliver that second shot on goal if you start on immunotherapy. Yeah, you can and them having high PD-L1 gives you a fighting chance, but if they aren't lucky and they decline rapidly, you may not ever get the chance to give chemo. So this is a situation where, yeah, you've got options, but I'd go for the more aggressive because you may only get one option.

**Dr. Piotrowska:** I think that's a very important point that we've seen across different studies, across different subtypes of cancer. That although we like to have many different lines of treatment, really that first line treatment is very important. There is a sub-set of patients who may not feel well enough to get later lines of treatment, a second line or third line therapy. So as much as you can give them the best treatment first, especially for someone like this who is so sick from their cancer, I think that gives you the best chance of success and the best chance of helping to turn that process around and get them feeling better.

END OF RECORDING