Case Based
Panel Discussions
Lung Cancer 2018

What is the Optimal Approach for a Fit Patient with Advanced Squamous NSCLC and Low Tumor PD-L1 Expression?

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TRANSCRIPT

Dr. West: Let's turn to squamous lung cancer. It's about a quarter of our patients with advanced non-small cell. It's the second-most common kind in the US and other parts of the world. This is a patient with a good performance status who has advanced squamous non-small cell lung cancer and does not have a driver mutation (these are not common in patients with squamous lung cancer) and has low PD-L1 expression. PD-L1 is the marker on cancer cells, the protein associated with a greater chance of responding to immunotherapy.

We now have a trial called Keynote-042 that was presented at ASCO 2018, our biggest cancer meeting of the year, that tested Keytruda as a single drug compared to chemo. We know this can be a very effective approach for the patients with high level PD-L1 of 50% or greater. But this study included patients with low PD-L1. That now opens it up to about two thirds of our patients with advanced non-small cell. And it included patients with squamous or non-squamous lung cancer.

So, there is that option. This did show a benefit. But it didn't look as good or as impressive in the patients with low PD-L1 like this patient. But we also saw some other trials at this same ASCO 2018 meeting that showed really impressive results with chemotherapy combined with immunotherapy, particularly a regimen of Carboplatin with either Taxol or Abraxane, a very related drug, as the chemotherapy that was significantly better when given with Keytruda compared to the same chemotherapy approach alone. So for patients with squamous lung cancer and low PD-L1, you could give Keytruda without the chemo or you could give chemotherapy with Keytruda; there was even some other work on other chemo and immunotherapy regimens that were maybe less impressive.

So, how do you sort this out as, you know, what bubbles up, what you would recommend for your patients if they come in with squamous and are fit and have low PD-L1. Zosia?

Dr. Piotrowska: So, the squamous data, you know, really combining chemotherapy and immunotherapy and comparing it to chemotherapy alone, was really promising, and it was exciting to see this data in squamous lung cancer. To say we've been a little bit behind adenocarcinoma in terms of treatment advances. I think that study was very similar and analogous to the Keynote-189 study that we had seen a few months ago where—

Dr. West: Which was in non-squamous lung cancer. And that was also chemo versus chemo with Keytruda.

Dr. Piotrowska: Mm-hmm. Similar concept – is it better to combine chemo and immunotherapy together versus just chemotherapy alone?

Dr. West: As the first treatment.

Dr. Piotrowska: As a first treatment for patients, exactly. And I think it's nice to see that in both studies, we really saw that the combination of chemotherapy and immunotherapy together was better than chemotherapy alone. To me, for patients with low level PD-L1 expression, I think that that combination is really better and more promising than immunotherapy alone for squamous cell patients. I think that for the low-level PD-L1 patients in the Keynote-042 study, like you mentioned, that data didn't look quite as good for the Keytruda given on its own. And so I think for the patients where they're fit and we think that they're candidates for the combination of chemotherapy are either with Carboplatin and Taxol or Carboplatin and Abraxane given in combination with Keytruda, I really do think that that is a very good treatment option and will become my standard of care for newly diagnosed squamous patients.

Dr. West: I was really impressed with – when we see these trials with immunotherapy we are used to looking at the difference of how do the patients with high level PD-L1 do? They typically get the biggest benefit. And then the lower and then the third of patients with no PD-L1. You know, how similar do they look? Or are the results really mostly due to the high PD-L1 patients perhaps dragging the others across the goal line too? But this trial, Keynote-407 of chemo with or without Keytruda for squamous was notable in showing that the patients, even with low or even negative PD-L1, showed the same trend of doing better – not just a trend but really a clear association of having the best results in overall survival, and time before the cancer progressed, and the probability of the cancer shrinking, all of those were better with chemo and Keytruda even if you had low or negative PD-L1. Taofeek, what do you think of all this?

Dr. Owonikoko: I think for a squamous patient, even though we have patients living with lung cancer, when we look at squamous lung cancer that's adenocarcinoma, I actually believe and I think that's the sentiment amongst all of us, these are two different diseases.

Dr. Piotrowska: Absolutely.

Dr. Owonikoko: And these populations of patients are also different. The type of treatment that they can tolerate is different and how they respond to treatment is different. Even if we just look at chemotherapy before the era of immunotherapy, we know that a patient with adenocarcinoma tends to respond better marginally to chemotherapy compared to a squamous patient.

And I think that is also what we're seeing with the Keynote-407 study; because the benefit of chemotherapy by itself in this subset of patients relative to adenocarcinoma subtype, it's probably a little bit lower, so we're able to see a higher magnitude of impact of either the immunotherapy to chemotherapy in this subset of patients.

For the example that we're talking about, where we have a fit patient with low PD-L1, I think the Keynote-407 for squamous patients actually makes the decision a little bit more difficult in the squamous population as to whether or not one should consider single agent Keytruda for this population of patient. So I am more inclined to offer my squamous patients the combination of chemotherapy and Keytruda, if there is no other contraindication to using it.

Dr. West: And importantly, we did see some other options. There was one of combination chemotherapy with a different immunotherapy Tecentriq that had some favourable findings, but it didn't show a survival benefit and my impression was it doesn't quite compare to the level of positive results we saw with the chemo and Keytruda combination here. Do you agree?

Dr. Piotrowska: Yeah, I agree. I think if we had seen that data in the absence of the Pembrolizumab or Keytruda data we would have been very excited. But I think given the very positive, and really not just positive for progression free survival or how long patients were able to stay on that treatment, but overall survival, which is really what we want to see, I think it's really hard to beat Keytruda currently in terms of becoming kind of the standard of care in combination with chemotherapy.

Dr. West: It's interesting because we have I think for the last few years considered these drugs way more similar than different, certainly in their – as single agents compared to Taxotere or Decotaxel or chemotherapy as second or third treatment. You know, these trials all showed very similar results with one or the other immunotherapy. I would largely consider them Coke or Pepsi or whatever. But with more of these trials we are seeing enough differences to lead us to step back and say, "I'm not so sure we should be that cavalier about just saying you should substitute one for the other."

Dr. Piotrowska: I think that's right. I think we have a lot more to learn, and there may be subtle differences, not just between the drugs themselves, but there are other factors that play into it. The drugs go along with the biomarkers that we use to test for them. So, we talk a lot about the level of PD-L1 expression (this protein that we look for in cancer cells). And that's tested for – you know, each drug has its own matched antibody that's actually used to test for this. And there may be differences not just between the drugs but also between the tests that are used to look for this PD-L1 expression, and those may be the reason why we see some of these differences.

There's also probably just differences among the patients on the studies, and it may not be that the drugs are really different but that the populations of patients included in each study were different. But I think that we are starting to see these differences in studies that are overall analogous (you know, the same concept but different drugs), and they don't always show the exact same result, which makes me wonder whether we really will see differences. And I think we need to study them further to understand that more.

Dr. Owonikoko: Yeah, I agree with Zosia on that. One of the other considerations that I've actually been struggling with for some time now, since all these data from the ASCO meeting came out is: For patients who have been previously treated and want to use immunotherapy, currently we have three options, only one of which requires the use of biomarkers. And I think most [sites, 9:44] have sort of gone with that to set up their system to test for that biomarker specifically for Keytruda. And the way the biomarker test is done, when you're talking of Tecentriq is somewhat different. So, that even if we have comparable results between the Tecentriq added to chemotherapy or Keytruda added to chemotherapy, because the biomarker selection is also different, it poses another layer of challenge in terms of what we do for patients on a day-by-day basis.

So [are we sure, 10:17] that our pathology colleagues would be able to set up another [... method] to look for the specific testing required for Tecentriq in addition to chemotherapy. I think these are things that we have to grapple with if these regimens also become a standard regimen that is approved by the FDA going forward.

Dr. Piotrowska: There's other factors that go into it. You know, these drugs are given at different frequencies, every four weeks, every three weeks, and so some of that will also – if we're really seeing studies that are in some way similar – those kind of factors will come into play. But I think right now I think we still need a lot more data to kind of parse out which of these drugs will be clearly the standard, and which ones we should definitely use going forward.

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