Case Based
Panel Discussions
Lung Cancer 2018

Metastatic Squamous NSCLC with Low Tumor PD-L1 Expression in a Frail Patient: What is the Best Treatment Approach?

Presented by Drs Zofia Piotrowska, H. Jack West, and Taofeek Owonikoko

TRANSCRIPT

Dr. West: The studies that we've seen with immunotherapy have really focused on patients with a good performance status, who are fit. And yet we have a lot of patients coming into our clinics who are more frail and are, arguably, maybe not as good candidates for treatment. So what would your approach be for a patient with a Stage-4 squamous lung cancer who has a low-level of PD-L1 (and that's, again, a protein on cancer cells, at least some patients, that is associated with a greater or a lesser chance of responding to immune therapy). And we have some options for patients, at least who are fit and strong enough to tolerate it and have low PD-L1 squamous lung cancer, no driver mutation. We have some evidence to support giving chemo with Keytruda, Pembrolizumab chemo. In fact, very good data. But we might be concerned about that being too much. We also have some evidence to support even giving Keytruda alone as an option. Keytruda was pretty much comparable to chemotherapy in another trial called Keynote-042, but it looked like the best results for patients were the ones who have high PD-L1, not as good with the low PD-L1.

So if you have a frail patient with squamous lung cancer and a PD-L1 level of 8%, how do you think you'd approach that kind of patient? Zosia?

Dr. Piotrowska: I think this is really where immunotherapy has been a big advance for us in the clinic. I think for the most part immunotherapy, especially when given alone, drugs like Keytruda or Opdivo, are easier to tolerate for patients than chemotherapy. We know that chemotherapy can be well-tolerated and certainly immunotherapy can have side effects. But if you look at all patients I would say, in general, immunotherapy is a little bit easier to tolerate and I think it's a very good option.

The Keynote-042 data that you mentioned did show that immunotherapy alone is a good option for patients who have any level of PD-L1 expression.

Dr. West: 1% or higher.

Dr. Piotrowska: Yes, 1% or higher. So anyone except for the less than 1%. And I think that this really gives us the opportunity to use immunotherapy alone for patients where we think that the combination of chemo and immunotherapy would be too much. And, as you say, I think that's a common scenario in the clinic. Many of our patients are older, they might have other medical problems, they might be more frail. And in those patients, I think immunotherapy alone can be a very good option, even for newly diagnosed patients.

Dr. West: Overall, we have discussed this in the context of patients who are stronger and felt that the evidence for chemo with Keytruda looked better than the evidence for Keytruda alone for the patients with low PD-L1, not as clear for the high PD-L1. But obviously there is the reality of what patients can tolerate. I think this is really an area of judgement and individual patient, both the individual doc and the individual patient. But do you have a sense of whether there could be – would you be inclined to do a modified lower dose of chemo with it to see whether chemo and lower dose, or is this the patient where you'd really favor trying immunotherapy and hoping you can get a good response and avoid chemo altogether?

Dr. Piotrowska: I would say that one of the challenges in particular with squamous cell lung cancer is that the chemotherapy medicines that we use for that sub-type of lung cancer are generally a little bit tougher to tolerate than the chemotherapies we use for adenocarcinoma. So the taxane-based chemotherapy sometimes can have a little bit more side effects than the Alimta, for example. I think that in particular has made me be a little bit more hesitant for the frail patient to use even dose-reduced chemotherapy. And I think, all things considered, I'm more inclined to use immunotherapy alone for the frail patient with squamous lung cancer, although I think there are individual cases where I might use dose-reduced chemotherapy together with immunotherapy. I don't know, Taofeek, what your experience has been?

Dr. West: What would you say?

Dr. Owonikoko: So, I agree with you. If you look at the lung cancer population as a whole, and I think we did this about ten years ago when we looked at the [SED database, 4:49]. About a third of our patients actually do not get treatment, half the diagnoses, because of other conditions that's going, co-morbidities, lack of access or whatever. So about a third actually do not get treatment. But for those who get treatment we know that chemotherapy can benefit them. And what we've done with frail patients in the past was to figure out a way to give the same chemotherapy that has been shown to be helpful in a fit patient to the frail patient. Either by giving it on a weekly basis, maybe giving one agent instead of two agents. So there is actually history of us trying to modify the standard chemotherapy in the frail patient as a way to bring the benefits to those patients who are not part of the clinical trial.

So fast-forward to the era of immunotherapy. The same thing is repeating itself now that we only allow very fit patients to come on all these studies. And now the majority of the patients seen in clinic are actually less fit than those that go on trial. So how do we then bring this to these patients as well? This is something that we all confront.

One approach that I've adopted is if you look at the Keynote-407 trial and the Keynote-042 trial, you have two options for patients with low PD-L1 expression, which is single-agent pembrolizumab or the combination of chemotherapy and immunotherapy. But for a frail patient we know that neither of these two options would be optimal. So what I've tried to do in some patients is after having a formal discussion and full disclosure with the patient, maybe start out with single agent immunotherapy. As Zosia said, that is more likely to be better tolerated than whatever type of strategy that we want to us with chemo.

Dr. West: A little different – you were favoring immunotherapy.

Dr. Piotrowska: Yeah.

Dr. Owonikoko: That's what I'm saying. So I will go with single agent immunotherapy in those patients. Now, one thing to also be aware of is there was a recent presentation by a group – I believe it was from Wake Forest – where they actually looked at frail patients and older patients (older than 70 years of age) and they gave them a combination of Keytruda and carboplatin paclitaxel on a weekly basis, the way we used to give the carboplatin paclitaxel in frail patients. And that was presented at the Santa Monica meeting in February this year. And they showed the response rate of about 70%. So why that is not the way the study was done, we actually now have investigators thinking of this as a real-world problem and trying to address it. So I think either we use single agent pembrolizumab and hope the patient is able to go through with it, and then maybe down the road, if their condition permits, you can bring back the chemotherapy to add onto it. Or you can do adjusted dose chemotherapy if the patient can tolerate it, along with immunotherapy.

Dr. West: Or you could consider maybe doing single agent with immunotherapy. I mean, the fact is we start out with evidence for the most fit patients without other medical problems, and that is only a sub-set of the patients in our clinic, and we have to make decisions with and for the patients who don't fit those criteria. And you can't just say, "Well, we have nothing for you. We don't have evidence." You do the best you can with judgements based on the discussion with the patient, and, as you said, full disclosure. I mean, you just clarify what we know and what we don't know.

What we can hope is, you know, these are still the very earliest days of these immunotherapy trials. And of course we get our first good evidence for the patients who are the most fit, but what I hope we find (I think we will in the next few years) is we'll fill in more of the gaps of the nuances of the more frail patients to help clarify that. It took a long time with chemo to get this kind of information, and we still make it up a bit as we go along. And I'm sure it'll take years to figure out the nuances with immunotherapy, including whether immunotherapy as a concept is as

effective in patients who are older and more frail, just because the immune system may not be as effective, but we'll learn more.

END OF RECORDING