Lung Cancer News and Updates ASCO 2020

Trial Updates-NSCLC

Trial Updates-Anti-TIGIT and NSCLC PDL1

The CITYSCAPE Trial-Adding Tiragolumab (Anti-TIGIT) to an Immune Checkpoint Inhibitor- A Better Treatment Option?

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Dr. Jack West: Hi, I'm Dr. Jack West and I'm associate clinical professor in medical oncology at the City of Hope Comprehensive Cancer Center, and also the founder and president of GRACE, global resource for advancing cancer education. I'm very happy to be joined today for an ASCO highlights presentation in the field of lung cancer with two of my friends and colleagues from other parts of the country who are lung cancer experts with some different perspectives. And we're going to go through some of the key presentations and talk about what we think this means for patients. So first I have Dr. Helena Yu, who is medical oncologist at Memorial Sloan Kettering Cancer Center and Dr. David Spigel, who is chief scientific officer and director of the lung cancer program at the Sarah Cannon Cancer Center in Nashville, Tennessee. Thanks guys for joining. Let's turn to advanced non small cell and immunotherapy.

And for several years, we've had immune checkpoint inhibitors, drugs like Keytruda, Tecentriq, and Opdivo some others, either alone or in combination with chemotherapy. And these have gone from being a second line or later treatment to increasingly used in the first line setting. But we are now asking whether we can potentially do better by adding drugs to that. And one of those is a drug called Tiragolumab, that targets a molecule called TIGIT or a pathway TIGIT. That this is essentially a way that conceptually was to try to make cancers that are not as immunoresponsive, immunosensitive, into more sensitive ones. And so this is an antibody it's given IV, and it blocks this pathway TIGIT and can lead ideally to greater immune sensitivity.

It was tested in the first line setting in a randomized trial, a phase two study with 135 patients who had PDL1 that marker we use for probable sensitivity to immune therapy. It was just looking for some degree of positive. So we have negative, and then we have

low PDL1 and the one to 49% range and then high in the 50% or higher range. And that's about a third of patients in each. So this is about two thirds of the population. This did not include patients with an EGFR mutation or ALK rearrangement, and this randomized patients to First Line Tecentriq, also known as Atezolizmuab, which was recently FDA approved in the spring of 2020 as a single agent approach for patients with high PD-L1, but not lower. Either giving that with placebo or with this novel agent.

And this study demonstrated an improvement in the response rate and well, and also the progression free survival when given as a combination, as opposed to the placebo. In fact, this is the pooled results for the low and the higher PD-L1. And it really looks for the benefit is overwhelmingly in the patients with high PD-L1. When they looked at it with updated results, you can see that the greater by far benefit in terms of response rate and progression free survival was really limited to the patients with high PD-L1. So I'm interested in your thoughts about this. It got some attention, but I think there's some skeptics about this. This is going to be followed up with a phase three, a larger study that is just focusing on this question and this combination in patients with high PD-L1. So I'll start with you, David. What do you think of this? Obviously it's not enough to say anything conclusive, but were you highly encouraged by this or anything else you know about this pathway?

Dr. David Spigel: Yeah. And I should disclose, we have been involved in some of this development, my colleague, Melissa Johnson, and colleague Joanna Bendale who actually just yesterday presented some updated data from kind of an all comer population in the plenary at ACR. So I don't know. I mean, I'm, you know, I have personal experience of well I have one patient doing very, very well on this. It reminds me of when nivolumab, ibilunimab was being developed and, you know, I do have some good, good results with that. So, I think we've all been waiting for the answer to something beyond chemo IO or IO with what we have, which right now in the first line setting is Atezo or Pembro in high expressing tumors. Nivo IPIs approval recently, which we may talk about in a little bit is the first IO, IO combination.

We all, you know, we all are familiar with many failed attempts. You know, speaking to the IDO experience that was very disappointing. This is the first one I've seen that could, that I think has some legs. And I think this kid, this kid moved forward, but you know, it's based on small numbers, the randomized phase three study is getting off the ground now. It's only, it's just been changed to non squamous high expressing patients just to kind of update you there. So it's going to be focused in that group because I think the greatest shot on goal was going to be in that group, but there's probably going to be additional work and in squamous cancer you know, if that hits, so this is one that I'm excited about. I don't think, you know, this should be any safer than say Nivo IPI. I think it's just going to be another regimen.

If I had to guess another regimen that could be active or more active than single agent therapy, the last thing I'll say, sorry, is the recent FDA approval of Atezo in the first line setting, which was instrumental to this trial because allows it to be the control arm in the phase three study. Whereas if it wasn't approved based on Empower 110, you'd have to use Pembro. And that, and that gets complicated doing a TIGIT, Atezo, versus a Pembro study. So it kind of all worked out for the development here, but we'll see what happens.

Dr. Jack West: And that was really just in the Nick of time because that approval was just 2 months, what are your thoughts here?

Dr. Helena Yu: Yeah. I echo everything that you and David said about this. I think it's early days, but you know, we all are looking for non chemo first line sort of options. And so, and I thought that obviously I don't have experience with this combination. But the talks that they presented seemed reasonable, obviously it's pretty early, but you know, I think, sort of, if you do a trial to trial comparison and it did seem like maybe it will have less toxicity than IPI Nivo, but who knows? I think, but yeah, I think it was the kind of sleepy hitter where we were, you know, people who weren't involved were sort of pleasantly surprised about the activity and we'll wait to see the phase three.