Lung Cancer News and Updates ASCO 2020

NSCLC Trial Updates - Checkmate 9LA

Opdivo (Nivolumab) and Yervoy (Ipilimumab) with Chemo vs. Chemo Alone for Treatment of PD-L1 Positive Advanced Non Small Cell Lung Cancer

Dr. Jack West, MD City of Hope Comprehensive Cancer Center, Duarte, CA. Founder, President, and CEO of GRACE

Dr. Helena Yu, MD Memorial Sloan Kettering Cancer Canter, NY, NY

Dr. David Spigel, MD Sarah Cannon Cancer Center, Nashville, TN

Dr. Jack West: Hi, I'm Dr. Jack West, 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 Spiegel, 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 pivot slightly.

And we have talked about the potential utility, but not a clear avenue to use of the combination of immunotherapy agents Opdivo, also known as nivolumab, and Yervoy, also known as ipilimumab, which had different targets in the immuno system, in our immune system surveillance for cancer. This study called Checkmate 9LA looked at the combination of Opdivo and Yervoy, but also giving concurrent chemotherapy for goals. And this was compared to chemotherapy alone for four cycles. And patients who had been squamous cancer could get alimpto or pemetrexed at maintenance. The study allowed patients with any degree of PDL, one expression from none to low to high.

So, the entire spectrum, and looked at overall survival as the primary end point that was being looked at. It did exclude patients with a driver mutation like EGFR or ALK. And we got some interesting news. We saw that we had heard a little before the actual meeting that this trial was positive. And then just days before the actual meeting and presentation of the data, the FDA approved it. Pretty unusual to have FDA approve a regimen before any of us have seen the data. So our first exposure to it was looking at

the package insert that accompanied the approval. But here's what we saw, a gap in the curves that shows a survival difference. And these data are not as mature as some of the other studies. We have patients who are just beyond a year and it's a two years.

And so, all of these circles on the bottom curve or triangles on the top curve represents patients at that point in time. So some projections of going to look in the future, but a suggestion here that there may be a prolonged survival benefit, possibly a subset of patients, even as high as 30 or more than 40% of patients doing well at 18 months to two years. And so this has kind of the best of both worlds or the worst of both worlds. It's a high powered immunotherapy regimen. And the idea of giving two cycles of chemotherapy with it was at this recognition that many of us have that it may take a period of time for immunotherapy to dig in its heels and turn the ship around. And the chemotherapy may be helpful in the beginning just to give it time to work.

And that is suggested by the curves that separate early, so that there really is at least some hint of separation from the beginning, favoring the combination that got two cycles of chemotherapy with the immunotherapy combination. And you could see that the benefit was present, whether patients had non-squamous or squamous histology, pretty comparable separation and improvement with the four drug regimen. And also that the benefit was seen everywhere in that PD-L1 spectrum from negative to low to high. So interesting results. And you know, you would expect that this is associated with some toxicity challenges, side effects now of both a pair of chemo agents and a pair of immunotherapy agents, but it's a short course of that before you stop the chemotherapy.

And the Yervoy, the ipilimumab also gets stopped after a limited period, so that the sustained treatment is just the Opdivo. So interested in your thoughts Helena, can you talk about, does this concept have any appeal to you or do you think it would have appeal to patients? Or we already have chemo immunotherapy with various regimens that give say chemo with Keytruda pembrolizumab, where might this fit in?

Dr. Helena Yu: So coming right off of discussing Checkmate 227, I really struggle even more to find a home for this regimen. I think that this is a trial where you really, if possible, would like to do that comparison to exactly, as you said, Jack to the pembrolizumab chemotherapy Keynote 189 study because, you know, I think this will surely add toxicity and it really is unclear whether there would be benefit, additional benefit. And I do think using two cycles of chemotherapy, you are potentially kind of wasting or possibly wasting you know treatment that you would like to use in the second line setting. So I don't see myself using this to any sort of significant degree,

Dr. Jack West: David, Helen has said that this might kind of burn a line of therapy by using the two cycles. I think one of the potential benefits of nivo IPI alone and arguably even with the two cycles of chemo is that it doesn't necessarily exhaust the benefit of a chemo combination in the second line setting. When otherwise, if we give chemo pembro, chemo, Keytruda, and patients are on that for some sustained period and then progress, you're left with more meager options. Does that hold water for you? Is there meaningful appeal to kind of saving something for later? Or are you more of a firm believer that you give your best treatments upfront because you just don't know what's coming after that?

Dr. David Spigel: Yeah, I mean, it's funny. I just recently heard that perspective and I hadn't thought about that. I could see why that's appealing because, you know, we do run out of things to do, but I, you know, I think, well with the three of us know too well is you never know what's going to happen with your patient, if they're ever going to make it to second line therapy. So I do kind of believe in using your best therapies early. So I have not used this regimen, but I'm intrigued by it for a couple of reasons. One is I love the idea of less chemo, if you can get away with it. I'm not a huge fan of, I mean, I do it. I give pemetrexed forever and, you know, I like the idea of giving less. And I know in this study they gave maintenance pemetrexed, but the concept of two cycles of platinum is appealing to me. It's this upper left corner that's interesting to me, the curves all look, but this group in particular looks very interesting because when you look at chemo and pembro in the zeros, or at least the low expressers, the benefit is not so clear.

And, you know what you're really getting, and there's been, this question of are the high expressers carrying all the benefit in our trials. This trial pretty clearly shows me benefit here in this group. And in 227, actually, we didn't spend a lot of time on it, in the zeros, although it's not FDA approved in that setting, that may be nivo Ipi greatest benefit is in the zeros. So I don't know, I haven't used this. I do think I'll try it. And I really like it for my low, my low expressers or zeros, but is it better than 189 or 407? Who knows? We don't know that. Is it more toxic? It seems like it's got to be you know, just because of the fact it's got a fourth drug in it.

Dr. Jack West: Yeah, it's interesting. I think a lot of people are most intrigued by the potential use of this nivo Ipi combo either on its own or with chemo in the low to negative PD-L1 group. We can, we're left with cross trial comparisons and inferences, and we could say, we want to see a trial comparing these, but I'm not sure that's the best use of patients, it's not going to lead to some quantum leap in how we manage patients. It's more of a, you know, a pretty minor one in the scheme of things. So I think we're just going to be left with our own judgment and talking with the patients about their preferences.

Dr. Helena Yu: I think one thing to add too, is I am actually interested in neither of these studies included that population, but thinking about immunotherapy, immunotherapy for potentially some of our mutation positive subgroups. And so I know there's a study ongoing of IPI nivo for EGFR mutant lung cancer. And so I think there is a real interest in potentially the dual immunotherapy being able to sort of harness the immune system in a traditionally old tumor, so that, we'll await those data.

Dr. David Spigel: Have you any kind of anecdotal experience there?

Dr. Helena Yu: I have seen some, I have not had personal anecdotal data, but there is some sort of anecdotal data out there that they're have been durable, significant responses in particular in EGFRs.

Dr. Jack West: Interesting. Yeah, that's a population that we just have so little data and plenty of patients are left, we're just grasping at straws.