Lung Cncer Video Library

General Non Small Cell Lung Cancer

Immunotherapy Combinations for Advanced NSCLC

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Dr. Benjamin Levy: I'm Benjamin Levy and I'm associate professor at Johns Hopkins School of Medicine. And we, over the past year or even six months have witnessed unprecedented advances for patients with advanced non small cell lung cancer, specifically for patients that are eligible for immunotherapy, and looking at the immunotherapy combinations that are approved, are being looked at, are being evaluated for patients. And I think what we've known prior to 2020 is that immunotherapy still remains a cornerstone treatment for patients without driver mutations. So these are patients that don't have, or are not eligible for targeted therapy. We know that there are a variety of different combinations that can be used. Probably one of the first ones that we knew about was a drug called pembrolizumab or Keytruda. And we know at least in some data as far back as five years ago, that pembrolizumab outperforms chemotherapy, specifically for patients with a PD-L1 greater than 50%.

And that's important. It must be tested. It must be greater than 50% in order to be used as a single agent. We've also learned that you can add a pembrolizumab to chemotherapy for patients with both adenocarcinoma and squamous cell, and that has a broad approval independent of PD-L1. So again, pembrolizumab can be used for a PD-L1 greater than 50% as a single agent, pembrolizumab can be used in combination with chemotherapy for all patients that are immunotherapy eligible with either adno or squamous cell. And in 2020 we saw new regimens, in addition to the ones that I've just shared with you, that are being approved or have been approved. One of the regimens that came out recently is the addition of atezolizomab in combination with carboplatin and nabpaclitaxel. Again, a very similar regimen as chemotherapy plus pembrolizumab.

This is yet another different immunotherapy added to a chemotherapy backbone that has shown improvements in survival.

So that regimen has been approved. But perhaps more recently, we've learned of two additional regimens that now have gained approval in 2020 that are beginning to alter the way we think about lung cancer and treat lung cancer. The first of these is looking at a chemo free regimen of ipilimumab and nivolumab. Nivolumab is a PD1 drug, ipilimumab is a CTLA 4 drug, as the class of drug both drugs or immunotherapies. But the combination of these drugs has not been approved in lung cancer up until recently. And the data that got these drugs approved is the study called the Checkmate 227. It was a trial that randomized patients with a PDL1 greater than 1% to these two drugs, immunotherapy drugs, and comparing the outcomes versus just standard chemotherapy alone.

And what we saw in this trial was an improvement, a market improvement, and overall survival by the use of these two immunotherapies, again, a chemo free regimen compared to chemotherapy alone. It showed improvements in survival at three years, for both those patients with a PD-L1 greater than 1% and a PD-L1 less than 1% when comparing this regimen to chemotherapy, as it currently stands, the FDA has approved this regimen of nivolumab. Plus it ipilimumab for patients with a PD-L1 greater than 1%. This does not take the place of other chemotherapy immunotherapy regimens or immunotherapy alone regimen. This is yet another tool or another combination that we have in our armamentarium. We don't know if this regimen is better than the other immunotherapy based regimens that are currently approved, but it is another option for our patients.

Specifically, patients that may not want chemotherapy. I think we need to be mindful that people, patients, this is chemotherapy free, so it must not have toxicities, but that is not true. This regimen of ipilimumab plus nivolumab does have significant toxicities that we need to be mindful of. And those include rash and diarrhea as well as inflammation of the colon and lung. So I am not currently using this regimen on all of my patients, but I think it is a consideration. The second regimen that was approved recently right around the same time that ipilimumab plus ipilimumab got approved, is a four drug regimen of chemotherapy for two cycles with ipilimumab plus nivolumab followed by ipilimumab plus nivolumab as just two agents after those two cycles. And this comes off of the Checkmate 9LA study, which was a very clean phase three study that randomized patients to standard chemotherapy versus chemotherapy backbone, plus it ipilimumab plus nivolumab.

So, a four-drug regimen. And we saw in all patients independent of what the PD-L1 status is from the tumor tissue, all patients derived a meaningful benefit and there was a survival advantage. And based on that, we now have an approval for this regimen as well. So there are multiple competing strategies, frontline options for patients without a

driver mutation. And I would just categorize these as either single agent or immunotherapy if the PD-L1 is greater than 50% chemotherapy, plus immunotherapy, single agent immunotherapy for all PD-L1s and patients with both adno and squamous cell. Immunotherapy combinations alone with ipilimumab plus CTLA 4 drugs ipilimumab plus nivolumab without chemotherapy. That's the third category. And then the fourth category is chemotherapy, plus ipilimumab, plus nivolumab, a four-drug regimen.

So, you can tell that things are getting very, very confusing also at the same time exciting. and I certainly think that you should be mindful of these four competing strategies. They've never been compared head to head. So we don't know which one of these is best. But this does allow us to reach into our toolkit and offer different regimens based on patient's symptoms, patient's performance status, and patient preferences. So I think these are really exciting times to be in the field of lung cancer. And I look forward to building on the science and the addition of new regimens in 2020 and 2021.