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When Adjuvant Immunotherapy for Resectable NSCLC May Be the Better Approach

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Dr. Donington:
Hello. This is CME on ReachMD, and I'm Jessica Donington. I'm a general thoracic surgeon and chief of thoracic surgery at the University of Chicago.

Today, I'm going to review and discuss the use of adjuvant immunotherapy in resectable non-small cell lung cancer.

The data for adjuvant immunotherapy has been out for several years now. It really comes from the IMpower010 and the PEARLS trial. We're both pretty familiar with these. These were for completely resected stage IA to IIIA lung cancer, and they received a year of immunotherapy or not. The main differences between these trials was in the use of chemotherapy.

Let's review the evidence here. It comes from the IMpower010 and the PEARLS/KEYNOTE trial. We are all fairly familiar with their schema. It was for completely resected patients. They received adjuvant chemotherapy and then went on to a year of immunotherapy. One of the key differences was that the adjuvant chemotherapy was only recommended in the PEARLS trial, and about 15% of patients didn't receive it. The other difference would be that the KEYNOTE trial used disease-free survival in the high PD-L1 expressors as one of their primary endpoints.

The results of these trials, I think, were also quite similar. And again, we've seen these curves for a while. The one on the left was the curve for the PD-L1-positive stage II to IIIA patients from IMpower, where the FDA approval was based. And the FDA approval for KEYNOTE was based upon the overall population with a hazard ratio of 0.76. And then that troublesome survival curve in those patients with high PD-L1 status, where the intervention arm just didn't perform as expected, and we've never fully understood why.

Regardless, we do have FDA approval for both of these agents. Atezolizumab received theirs first for the PD-L1 positive II to IIIA patients. And then pembrolizumab got the broader approval. Pembrolizumab received theirs later, but with the higher hazard ratio here, I think there's less enthusiasm for its use.

At ASCO this year, Heather Wakelee provided us with an update on the IMpower010 trial, now with follow-up through 5 years. This is the final DFS [disease-free survival] analysis, although they will continue to follow for overall survival. In general, we see that the disease-free survival benefit continues and it does translate to an overall survival benefit, but only in those patients who are PD-L1 positive. If you look at the PD-L1-positive stage II to IIIA, we see a disease-free hazard ratio at 0.70 and an overall survival hazard ratio at 0.77. When you look at those high expressors, those get even better with a hazard ratio of 0.49 for disease free-survival and 0.44 for OS [overall survival]. So pretty impressive in that population. They did not see significance for the disease-free survival in the intention-to-treat population.

So where does this fit into our very complex perioperative schema? Well, clearly for those patients who did not see induction therapy, I

think this is a home run, especially for the PD-L1 high expressors. If I have a patient who I know is stage II or III and has PD-L1 expression, would I choose this first? Probably not. But we must remember that lots of patients go to the OR as stage I and then come out upstaged to stage II or IIIA, and I think this is a perfect option for those patients who are PD-L1 positive.

Our time is up. I hope you find this information presented here helpful to your practice. And thank you for listening.

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