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Perioperative Immunotherapy for Resectable NSCLC: Evaluating Approved and Emerging Approaches

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Awad:
This is CME on ReachMD. I'm Dr. Mark Awad, and today I'm going to review and evaluate some of the approved and emerging neoadjuvant and perioperative chemoimmunotherapy approaches for patients with resectable non-small cell lung cancer.

This has been a rapidly evolving landscape for our patients, and as you can see, a number of trials have been reported leading, in many cases, to FDA approvals. We have adjuvant-only immunotherapy approvals, namely the IMpower-010 trial of adjuvant atezolizumab and the KEYNOTE-091 trial of adjuvant pembrolizumab. We have the neoadjuvant-only chemoimmunotherapy approach of chemotherapy plus nivolumab for 3 cycles followed by surgery from CheckMate 816. And now we see a number of emerging and approved perioperative strategies using chemoimmunotherapy before surgery followed by adjuvant immunotherapy, in most cases, after surgery.

It's important to note when we try to look across these trials, while many of them have roughly similar trial designs, there are some important differences in how these trials were conducted and in which parts of the world. The CheckMate 816 trial, again, was our neoadjuvant-only trial, and then KEYNOTE-671, AEGEAN, CheckMate 77T, and Neotorch are our perioperative studies. Many of these were global studies. The Neotorch study was conducted in China mostly. And there are some differences in the patient populations in terms of the histology rates of squamous versus non-squamous non-small cell lung cancer, the trial size, the percent of patients with stage II versus III disease, but overall, you can see that the pathologic complete response rate [pCR] for patients receiving chemoimmunotherapy ranged from about 17% or 18% to up to 24% or 28%, which is impressive for this population. We can also see event-free survival hazard ratios all favoring the use of neoadjuvant chemoimmunotherapy, as well as benefit, potentially, for the use of adjuvant immunotherapy in these perioperative studies.

It's important, of course, to discuss the potential for low-grade but also high-grade adverse events. And here we can see the percent of grade 3 or higher adverse events, as well as the grade 5 deaths that were reported in these studies. And in general, most patients have been able to get through treatment relatively well, although these are important discussions that have with our patients in clinic. And a number of these trials have already been FDA-approved or will be reviewed by the FDA in the coming months.

When we look across these trials at what's been known for overall survival, it's important to note that a lot of these are interim analyses, but we can see that the hazard ratios favor the use of, at least, neoadjuvant chemoimmunotherapy. If you look at trials such as CheckMate 816, KEYNOTE-671, Neotorch, and others, we can see that the overall survival hazard ratios really favor the use of these approaches. By contrast, with the adjuvant-only immunotherapy trials, like IMpower-010 or KEYNOTE-091, we can see that the overall survival hazard ratios really don't show a strong benefit yet to date for patients receiving adjuvant immunotherapy.

So I think for these reasons, when we talk to our patients in the clinic, for the right patient in the right setting, we really do try to favor at least neoadjuvant chemoimmunotherapy, if not that plus adjuvant immunotherapy.

This next slide summarizes a comparison of the pathologic responses across these trials. And again, you can see fairly similar pathologic complete response rates for patients receiving chemoimmunotherapy across CheckMate 816, as well as these 4 perioperative studies, with the pCR rate ranging from 17% up to about 25%. By contrast, for patients receiving chemotherapy only in the neoadjuvant setting, the pCR rate is quite low, 1% to 4%. Similarly, the MPR [major pathologic response] rates are significantly higher among patients receiving neoadjuvant chemoimmunotherapy as compared to chemotherapy alone.

And lastly, it's important to consider the surgical outcomes for patients receiving immunotherapy. Across these trials, there are patients that don't make it to surgery, and that's a very important consideration, raising the question: Are there some patients that should proceed straight to surgery rather than receiving chemoimmunotherapy, or, really, do you need an understanding of what are the characteristics for patients that don't make it to surgery? But in general, you can see that patients receiving chemoimmunotherapy have a very good rate of successful surgeries, as well as R0 resection. And for these reasons, again, in the right setting, we really do favor the use of chemoimmunotherapy in the neoadjuvant setting for our patients.

Our time is up. I hope you have found the information presented in this episode helpful to your practice. Thank you for listening.

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