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Consolidative Immunotherapy in Unresectable Stage III NSCLC With Oncogenic Drivers

Announcer:
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Dr. Reuss:
This is CME on ReachMD and I'm Dr. Joshua Reuss, and today we're going to be discussing consolidative immunotherapy in unresectable stage III non-small cell lung cancer with oncogenic driver mutations. Really pertinent topic here.

We know that in the metastatic setting, patients with oncogenic driver mutations, at least a large percentage of these subgroups, do not benefit from immunotherapy. And in these patients, actually, appropriate targeted therapy is our frontline treatment strategy, with immunotherapy playing a limited role outside of clinical trials. So it's only natural to explore this further in patients with unresectable disease who have received definitive chemoradiation, and we are considering for adjuvant durvalumab immunotherapy.

We know that for some of these subgroups, such as the EGFR mutation subgroup, there is limited subgroup data from the PACIFIC trial and from real-world analyses to suggest that, like in the metastatic setting, there is limited utility for durvalumab. And in my practice, I will not typically offer adjuvant durvalumab immunotherapy and will entertain off-label use of adjuvant osimertinib, kind of mirroring an ADAURA trial, ADAURA paradigm, where patients with resected disease will receive adjuvant osimertinib. However, we know that this hopefully won't be an off-label approach for long. We recently saw there was a press release from the phase 3 LAURA trial that randomized patients with classical activating EGFR mutations following chemoradiation to adjuvant osimertinib or placebo. And we found that this actually was a positive study with a positive progression-free survival endpoint.

Then there are other subgroups where we also know immunotherapy has limited benefit. For example, ALK fusion, RET fusion, ROS1. I think in these subgroups there's many variables that need to be considered when thinking about the appropriate adjuvant therapy. And in these subgroups, I typically would not offer adjuvant durvalumab. In some where there is an effective targeted agent that has a good safety and tolerability profile, for example, our ALK fusions and RET fusions, I oftentimes will consider an off-label use of a targeted agent because we need to be confident that a patient's going to be able to tolerate the therapy for at least 2 or 3 years or beyond, if that is an approach that we're going to consider. Because there are other mutations, for example, I think ROS1, MET exon 14, where I'm a little skeptical if a patient's going be able to tolerate the therapy for that length of time given the toxicity profile. In addition, for some of these mutations, I think the lack of immunotherapy benefit is less clear. For example, a Met exon 14 skipping alteration or a non-BRAF V600E that has a prominent smoking history, perhaps a HER2 mutation with prominent smoking history, you know, I think these are patients where I wouldn't necessarily take immunotherapy off the table, and I would look at patient-specific factors, co-mutational profile, other things to try to determine if immunotherapy is the most appropriate strategy over observation.

And then, of course, there are mutation subgroups where we know there is a benefit to immunotherapy, most notably KRAS, which is seen in probably 30% to 35% of advanced non-small cell lung cancer diagnoses. We know there's benefit for immunotherapy-based strategies in the metastatic setting, and subgroups analysis from locally advanced unresectable disease suggest benefit for immunotherapy after chemoradiation as well. And so this is a patient population where I absolutely would move forward with adjuvant

durvalumab immunotherapy if it is otherwise clinically appropriate to do so.

So with that, I think that was a lot of information in just a few short minutes to digest, but I want to thank you for your time and for your attention.

Announcer:
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