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The Current Therapeutic Landscape in Unresectable Stage III NSCLC

Announcer:
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Dr. Liu:
Welcome to CME on ReachMD. I'm Dr. Stephen Liu, and joining me today, Dr. Joshua Sabari, Dr. Susan Scott, to discuss the current therapeutic landscape in unresectable stage III non-small cell lung cancer.

Susan, can you kick off today's discussion by reviewing guideline-endorsed approaches in this setting?

Dr. Scott:
Yes, absolutely. So our current approach for stage III unresectable non-small cell lung cancer is to use concurrent chemoradiation followed by consolidation immune checkpoint inhibitor. Currently approved is durvalumab. So this comes from the PACIFIC study, which we'll go through. But this is our current approach. It is PD-L1 agnostic. We do not use it for or tumors with EGFR driver mutations, which have alternative approved therapies.

The other driver mutations are a bit of a mixed bag. We don't have studies for each of them to know what to do. Currently, they're eligible for durvalumab, but that's definitely a place of kind of unmet need, as well as looking for anybody that might need escalation of care in this setting. We use it in PD-L1 negative tumors as well as PD-L1 positive. And these are some areas where we're really trying to refine our approach.

But currently, most everybody gets consolidation durvalumab following chemoradiation.

Dr. Liu:
And we know that the PACIFIC trial, a randomized phase 3 trial, showed an improvement in progression-free survival and improvement in overall survival. We have 5-year survival data really showing the benefit of giving durvalumab after chemoradiation for unresectable stage III non-small cell lung cancer.

Josh, we also have a pretty robust real-world study. Can you briefly review the data and long-term follow-up from PACIFIC-R?

Dr. Sabari:
Yeah, I think real-world data is important here, right? A lot of controversy about study population being very fit. What does this concurrent chemo RT followed by durvalumab look like in the real-world population? International observational study, many patients enrolled, and we recapitulated very similar data. So 5-year overall survival on the real-world study, 49.2% so hovering right at that 50% rate. And we look at the 5-year real-world progression-free survival, about 32.5%, so encouraging outcomes observed, again, across all subgroups, supporting the use of the PACIFIC regimen.

The one thing I'll point out Susan mentioned is the EGFR-mutant population and maybe other driver-altered populations such as ALK,

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RET, ROS, never smokers, those patients really did not seem to benefit from this approach.

Dr. Liu:
Yeah. I mean those estimated 5-year survival rates with durvalumab from PACIFIC, 42.9%, so even better in some real-world populations. I think these are really encouraging. Often, when we look at real-world data, we see a big drop-off. We didn't really see that with PACIFIC. And so Josh, what's been your personal experience with the application of these data off study and in practice?

Dr. Sabari:
Yeah, I'll tell you early on, going back to 2018, there's a lot of learning on how to do concurrent chemo RT followed by durvalumab — when to get the scan, how to manage the toxicity. Now, it's very commonplace, right? All clinicians are using this regimen, so I think it's exciting to see in the real-world analysis, which happened later from the data we collected on trial. I think we all feel comfortable, confident using consolidation durvalumab post concurrent chemo RT.

Dr. Liu:
Yeah. Susan, your personal experience?

Dr. Scott:
Absolutely. I use it all the time, and I'm hopeful that it's making a big difference for many of my patients.

Dr. Liu:
Yeah, completely agree. I think one key point that we've all sort of mastered is the need for that EGFR/ALK testing up front. And because we're in the radiation setting, we want to do that testing on a sample that hasn't been radiated. If we wait until after chemoradiation, often there's not really any viable tumor to biopsy, so we want to be sure our colleagues are getting enough tissue to do that testing really from the jump.

Josh, Susan, great insights to wrap up this brief discussion. Thanks everyone for listening.

Announcer:
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