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Immunotherapy Approaches in Unresectable Stage III NSCLC: What's on the Horizon?

Announcer:
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Dr. Gray:
Hi, this is CME on ReachMD and I'm Dr. Jhanelle Gray. There are numerous ongoing clinical trials investigating immunotherapy approaches in unresectable stage III non-small cell lung cancer. Let's take a look at a few of them.

So we have the PACIFIC study that we know from the 3- and the 5-year update, we had improvement in overall survival as well as progression-free survival with consolidation durvalumab following concurrent chemotherapy and radiation therapy. More recently, we've had evaluation of consolidation durvalumab after sequential chemoradiation therapy in the PACIFIC-6 study. There was actually a low percentage of patients with ECOG performance status 2 and, of note, PD-L1 status was unknown in 40% of the patients. The median overall survival on this study across all comers was 39%, and progression-free survival median was 13.1 months.

We also have the PAC[IFIC]-5 study, which is now looking at either concurrent chemoradiation or sequential chemoradiation followed by durvalumab versus placebo. Primary endpoint is progression-free survival, and we look forward to hearing those results.

What about combining immunotherapy with concurrent chemoradiation? This is moving it up front earlier now in the treatment. In addition to that, there's also some trials looking at induction chemotherapy and immunotherapy followed by chemotherapy and radiation therapy with the immunotherapy and followed by the immunotherapy consolidation. This is exactly the KEYNOTE-799 study, which has a cohort of squamous and nonsquamous, as well as a Cohort B of nonsquamous only. The median progression-free survival in those with squamous and nonsquamous who received carboplatin and paclitaxel as their chemotherapy was 30.6 months, versus those who had a nonsquamous histology, the median progression-free survival was not reached. We also saw the data from the PACIFIC-2 study in patients with locally advanced unresectable stage III non-small cell lung cancer that was presented by Jeff Bradley more recently at ELCC [European Lung Cancer Congress]. Unfortunately, this was not reached, with a hazard ratio of 0.85. The overall survival hazard ratio was 1.03. When we look at why we think this occurred, we think the patient population had something to do with this. Majority of patients were Asian. There was a significant amount of patients that had unknown EGFR status, and there was also patients from South America that did not appear to benefit.

We also have the ECOG clinical trial which is also moving up the durvalumab with the concurrent chemoradiation followed by durvalumab consolidation, versus the PACIFIC arm. We eagerly await results of this clinical trial as well.

What about combined immunotherapy, now, following concurrent chemoradiation? We've looked at this with ipi and nivolumab in combination following concurrent chemoradiation versus nivolumab alone. I think the key take-home message here is there's no real change in the median overall progression-free survival nor the 18-month or 24-month overall survivals, and the treatment-related grade 3 toxicities were worse with the ipi/nivo.

We also have novel therapies that we're evaluating in this setting. We have the COAST study, which showed that oleclumab in

combination with durvalumab, or monalizumab, which is an anti-NKG2, in combination with durvalumab was superior in a phase 2 study to durvalumab alone. There are also no unmasked adverse events that weren't previously known and no increased rates of pneumonitis that appeared significant.

We also have studies such as the SKYSCRAPER-03, which is looking at consolidation therapy with tiragolumab, an anti-TIGIT, and atezolizumab. We have the KEYLYNK-012 study, which is looking at concurrent chemotherapy and radiation therapy plus pembrolizumab, followed by consolidation with a PARP inhibitor plus pembrolizumab.

Interestingly, one of the questions that comes up is when to start to up durvalumab after chemoradiation. We have the DATE study also, which looked at durvalumab days 1 to 5 starting after completion of chemoradiation. And when we look at this study, we have to note that the any-grade pneumonitis occurred at 78%, and the grade 3 pneumonitis was at 4.3%. We need to look at these information and these comparisons within one study with comparison arms.

So to summarize, there's numerous trials currently ongoing looking at immunotherapy combination strategies in the consolidation setting, moving up the immunotherapy with concurrent chemoradiation, and we eagerly await the results of all of these studies that are ongoing. I hope that you find this brief report helpful and useful. And my time is up, but thanks so much for listening.

Announcer:
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