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TROP2-Directed ADCs in Lung Cancer

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum and is titled “TROP2-Directed ADCs in Lung Cancer”.

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Dr. Gainor
This is CME on ReachMD, and I'm Dr. Justin Gainor, director for the Center for Thoracic Cancers at the Massachusetts General Hospital and an associate professor of medicine at Harvard Medical School.

Today, we'll be discussing TROP-2 antibody-drug conjugates. One of the major unmet needs in non-small cell lung cancer is to find effective therapies for patients after progression on platinum-doublet chemotherapy and immune checkpoint inhibitors, particularly among patients who do not have a targetable genetic alteration. Within these patients, what we've found is that non-small cell lung cancers commonly overexpress new targets such as TROP-2. And this could be an ideal target for an antibody-drug conjugate in these patients.

To date, we've seen data in non-small cell lung cancer with 2 different TROP-2 antibody-drug conjugates, the first being datopotamab deruxtecan or Dato-DXd. And this agent was being explored in the TROPION-PanTumor01 study. In this study, the antibody-drug conjugate was being explored in both dose-escalation as well as dose-expansion portions of this study.

Select treatment-emergent adverse events grade 3 or higher included things like decreased neutrophil count, which was found in about 1%. All grade was more on the order of 6%. Diarrhea was seen in approximately 6% of patients. Drug-related interstitial lung disease by independent adjudication was one of the noteworthy adverse events seen in 11% of patients on this study. Notably, at the highest dose level of 8 mg/kg, this was seen in 15% of patients. So that is one of the adverse events that clinicians should be mindful of, particularly in a non-small cell lung cancer patient population. Altogether, dose reductions occurred in 16% of patients, and dose interruptions occurred in approximately 18% of patients. In total, 15% of patients discontinued therapy due to treatment-emergent adverse events.

In parallel with the clinical development of Dato-DXd, we've seen data with sacituzumab govitecan. This is an agent that is now FDA-approved in the treatment of metastatic breast cancer and is now being explored in non-small cell lung cancer.

So far, it seems like TROP-2 expression by itself is not a biomarker of activity within non-small cell lung cancer. In preliminary studies using sacituzumab govitecan, grade 3 adverse events included neutropenia in about a quarter of patients, pneumonia in approximately 10% of patients, diarrhea in 7%, and nausea and fatigue in approximately 6% to 7%.

Adverse events appeared to be similar at the 2 dose levels that were explored, except for an increase in grade 3 or 4 neutropenia at the highest of the 2 doses tested. So this was 30% versus 13%. Ultimately, adverse events led to drug discontinuation in 2 patients. This was for grade 3 pneumonia and grade 3 recurrent pruritus.

Currently, we don't have any TROP-2 ADC that is FDA-approved in non-small cell lung cancer, though the data thus far has been quite encouraging, especially when put into the context of other disease settings such as the activity of sacituzumab govitecan in breast

cancer. We're going to take some of the lessons from other disease areas as we start thinking about how to manage some of these adverse events. We'll also need to place this in the context of how we manage toxicity from cytotoxic chemotherapy such as dose interruptions, dose reductions, particularly around things like cytopenias. When we do see interstitial lung disease, having a low bar to interrupt therapy, reach out to our pulmonary colleagues, and introduce steroids if we do observe that, recognizing that non-small cell lung cancer patients may have multiple reasons to develop interstitial lung disease, so having a high level of suspicion for these patient populations.

As with other agents used in a non-small cell lung cancer patient population, employing a multidisciplinary approach will give our patients the best opportunity to have these adverse events managed most effectively.

Announcer:
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