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Optimal Management of ADC-Related Gastrointestinal AEs in NSCLC

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

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Dr. Smit:
This is CME on ReachMD, and I'm Dr. Egbert Smit from Leiden University Medical Center in the Netherlands. Today, I'll take you through the best practices for managing GI toxicities related to antibody-drug conjugates, or ADC, therapy in non-small cell lung cancer.

We'll start with trastuzumab deruxtecan, which is currently the only approved ADC for non-small cell lung cancer for patients with HER2 mutations. And later, I will briefly review the investigational ADCs for lung cancer.

So as you are aware, trastuzumab deruxtecan consists of a monoclonal antibody, trastuzumab directed against HER2, a linker, and attached to the linker are the cytotoxic compounds, which is in this case deruxtecan, a topoisomerase I inhibitor.

In the phase 2 studies that have been conducted with trastuzumab deruxtecan and reported in the DESTINY-Lung01 and Lung02 trials, the number of patients that experienced GI [gastrointestinal] toxicity of any grade was approximately two-thirds. However, the higher-grade toxicities were actually quite low.

It's also important to remind you that there are 2 doses of trastuzumab deruxtecan tested in the DESTINY-Lung01 and 02 study which was the 6.4-mg/kg dose administered every 3 weeks and the 5.4-mg/kg dose administered every 3 weeks as an IV infusion. The latter dose is used more often in patients with breast cancer. But the initial dose of trastuzumab deruxtecan tested against non-small cell lung cancer, based on the results that were obtained in the phase 1 study, was 6.4.

If you look at the results that have been reported in the randomized phase 2 study, where the 2 doses were compared to each other, the result of the study showed that the efficacy of the 2 doses were the same. We might note that the number of patients that had nausea was about two-thirds, one-third of the patients had vomiting, and about one-fifth of the patients had diarrhea and one-third of the patients had constipation.

I think the management of these mostly lower-grade toxicities, because a majority of these toxicities were grade 1 and 2, is important so that patients can stay for a long time on treatment. As you may recall, the median progression-free survival of patients treated with trastuzumab deruxtecan was approximately 8 or 9 months. So patients need to be comfortable with respect to GI toxicities.

There are a couple of guidelines that are reported in the literature. And based on the current guidance, nausea and vomiting may be treated with prophylactic serotonin receptor antagonists and dexamethasone and appropriate antiemetic regimen with neurokinin 1 receptor antagonists and olanzapine for breakthrough or severe nausea or vomiting. And, of course, there are protocols for managing diarrhea and constipation that are appropriate for patients that are treated with topoisomerase I inhibitors.

What do we know about the investigational ADCs? There are a couple of them; datopotamab deruxtecan, which was tested in the TROPION-Lung01 study, had a 50% rate of stomatitis, which I think is troublesome for these patients. And patritumab deruxtecan,

tested in the HERTHENA-Lung01 study, virtually all patients had lower-grade toxicities, including nausea and vomiting in about two-thirds and one-third of the patients. And these can be managed in the same way as patients treated with T-DXd.

So thanks for listening and I hope this overview will be helpful in your practice.

Announcer:
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