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https://reachmd.com/programs/cme/her3-directed-adcs-in-lung-cancer/13888/

Released: 06/30/2022
Valid until: 06/30/2023
Time needed to complete: 1h 01m

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HER3-Directed ADCs in Lung Cancer

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum and is titled “HER3-Directed ADCs in Lung Cancerr”.

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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 HER3-directed antibody-drug conjugates in the management of EGFR-mutant non-small cell lung cancer.

The current standard of care for patients with newly diagnosed EGFR-mutant non-small cell lung cancer is treatment with third-generation EGFR-targeted therapies. Unfortunately, patients will invariably develop resistance, at which time we have more limited options. Over the last decade, we've come to gain insights into mechanisms of resistance and recognizing that HER3 signaling may play a role in resistance and be upregulated among patients with EGFR-mutant non-small cell lung cancer.

And this is really the basis for the clinical development of patritumab deruxtecan, otherwise known as HER3-DXd. This agent was explored in the phase 2 HERTHENA-Lung01 study, specifically among patients with EGFR-mutant non-small cell lung cancer after disease progression on targeted therapies. Within this study, treatment-emergent adverse events occurring in greater than 5% of patients were reported at ASCO 2021. Altogether, 81 patients were treated with HER3-DXd in this study. The most common grade 3 or greater adverse events included alterations in platelet count and neutrophil count.

Typically when I encounter cytopenias, whether it be from chemotherapy or antibody-drug conjugates, I manage those the same way, which is typically with dose holds and dose reductions if needed, since there are off-target effects, bystander effects, and we certainly see cytopenias with antibody-drug conjugates.

Other adverse events observed in this study that were grade 3 or greater were things such as fatigue, which was around 5% to 10% of patients, as well as shortness of breath and febrile neutropenia, which were more on the order of 5%.

Obviously, when patients are reporting shortness of breath, one wants to be on the lookout for reasons for the shortness of breath, particularly in a lung cancer patient population. You want to look for interstitial lung disease because that's been reported with other antibody-drug conjugates. And looking to make sure that, you know, it's not anemia or other things that are contributing to that shortness of breath.

Ultimately, with antibody-drug conjugates, just as with other therapies, that when patients are encountering adverse events, it is important to deploy a multidisciplinary team, including engaging our pain and palliative care colleagues to help us manage the toxicity related to these agents.

Announcer:

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