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Emerging ADC Therapies for NSCLC: Anticipating AEs Reported in Clinical Trials

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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. In this episode, we'll review the emerging antibody-drug conjugates, or ADC, therapies that are under investigation in non-small cell lung cancer.

For those of you that are active in the field of thoracic oncology, it's no news that patients will inevitably progress even after treatment with monoclonal antibodies directed against the PD-1 or PD-L1 axis or after therapy on cytotoxic agents, and there is a need for newer and more effective therapies with particularly manageable toxicities, and there's a potential role for ADCs in this setting, and therefore, it's important to know the individual side effects of emerging ADCs to use them safely once they are approved.

I think the 2 most important investigational agents in non-small cell lung cancer when it comes down to the ADCs are datopotamab deruxtecan. It's an ADC where the monoclonal antibody is directed against TROP2. TROP2 is a protein that's almost ubiquitously expressed in cancer and to a far lesser extent in normal tissues.

In the phase 1 and also in the phase 3 studies that are already conducted with datopotamab deruxtecan, there was a very low cardiac AE incidence. The number of patients that developed interstitial lung disease was also much lower as compared to trastuzumab deruxtecan in patients treated with Dato-Dxd, and the adjudicated drug-related ILD grades 3 or more was only 3.4%. However, the principal toxicity of Dato-DXd is GI toxicity, including stomatitis, in approximately half of the patients. Although it is small, mostly grade 1 and 2, for patients, this can actually be quite troublesome when they are on treatment for a long time. And I think the most relevant toxicity of this compound is indeed the stomatitis.

The management for these side effects are whatever one does for stomatitis in the context of treatment with cytotoxic agents. Some investigators in the TROPION-Lung studies reported that ice chips in the mouth during the infusion of Dato-Dxd was helpful in order to prevent the occurrence of stomatitis.

The other next important ADC that is developed in non-small cell lung cancer is patritumab deruxtecan. It's an ADC where the monoclonal antibody is directed against HER3. Cardiac toxicities are virtually nil, and the ILD adverse events are also of low incidence and is in the order of a few percent of patients but still a relevant toxicity to look for.

I think the principal toxicities of this compound, patritumab deruxtecan, are GI toxicity, particularly nausea and vomiting, which is in approximately half of the patients relevant. And this compound carries a hematological toxicity rate in the order of 35% for neutropenia and thrombocytopenia of 40%. And the management of these AEs are not really different from management with other cytotoxic compounds.

As you are probably aware, there are other ADCs in development in non-small cell lung cancer, and some of them did not make it or were halted in phase 3 development. For instance, sacituzumab govitecan was faced with a negative result of a phase 3 study. But

there are some others that are coming up and I think are of interest. And particularly, ifinatamab deruxtecan, which is directed against CD-47, I think, is a compound to keep an eye on.

And that's all the time I have. And I hope I gave you something to think about. And thanks for tuning in.

Announcer:
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