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TROP2-Directed ADCs in Breast Cancer

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

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Hurvitz:
This is CME on ReachMD, and I'm Dr. Sara Hurvitz, Professor of Medicine and Medical Oncologist at UCLA.

The treatment of triple-negative breast cancer has dramatically changed recently, not only by the availability of immune checkpoint inhibitors and PARP inhibitors for select patients, but also by the development and approval of the first antibody-drug conjugate [ADC], sacituzumab govitecan, for metastatic triple-negative breast cancer.

This drug selectively delivers chemotherapy to an antigen known as TROP-2, which is expressed on cancer cells.

More recently, early clinical data is emerging relating to the antitumor activity of another TROP-2-targeted ADC, datopotamab deruxtecan, or Dato-DXd. While these agents have both demonstrated impressive antitumor effects, they have unique side effect profiles to be aware of as well.

The first ADC to be approved for metastatic triple-negative breast cancer is sacituzumab govitecan, a TROP-2-targeted agent that delivers a topoisomerase-1-directed cytotoxic payload to tumor cells. This drug was shown to significantly improve progression-free and overall survival compared to single-agent chemotherapy in the third-line setting and beyond in the ASCENT phase 3 clinical trial leading to its FDA approval in 2019.

While its antitumor effects are impressive, the off-target toxicity associated with this agent includes significant neutropenia, including febrile neutropenia, as well as GI toxicities such as diarrhea and nausea. Additionally, patients will likely experience full alopecia with this agent.

Use of white cell growth factors should be considered and may be useful in managing the hematologic toxicity associated with this agent. Moreover, patients should have antimotility agents on hand at home in case they experience diarrhea and should be in close communication with their physician or other providers. On occasion, consultation with a GI specialist is useful in cases of severe diarrhea.

At ASCO 2022, we are hearing more about this agent, sacituzumab govitecan, as phase 3 data will be presented relating to the use of this drug in hormone receptor-positive HER2-negative metastatic breast cancer.

Datopotamab deruxtecan, or Dato-DXd, has not yet been approved, but is demonstrating interesting antitumor benefits in a phase 1 clinical trial called TROPION-PanTumor01.

In addition to antitumor benefits, it is showing toxicity profiles that we need to be aware of including nausea. In addition, this agent has

been associated with stomatitis and fatigue. Patients may experience cytopenias with this agent. So again, growth factors might be useful in helping to manage this particular side effect. More data is expected and eagerly anticipated to fully understand the safety profile of this agent in breast cancer.

So that's all the time we have for today. TROP-2-directed ADCs have hit the scene for treatment of triple-negative breast cancer. The efficacy data associated with sacituzumab govitecan is extremely exciting, but clinicians need to be informed about the potential toxicities associated with this agent in order to optimize outcomes for their patients.

In some cases, multidisciplinary management of adverse events is needed, most notably from our colleagues in gastroenterology.

Thank you so much for your attention. We hope this was helpful.

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