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HER3-Directed ADCs in Breast Cancer

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum and is titled “HER3-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 breast cancer has been revolutionized by the development of therapies that specifically target antigens that are expressed uniquely or at a high level on the surface of tumors. Antibody-drug conjugates, which selectively deliver chemotherapy to tumor antigen-overexpressing cancer cells, have demonstrated significant antitumor efficacy in HER2-positive breast cancer and triple-negative breast cancer.

The development of ADCs, or antibody-drug conjugates, is now expanding to other tumor antigens. For example, to HER3, making this field extremely exciting. While data are quite promising, there are unique side effects to be aware of as we see these agents enter later-phase clinical trials.

One agent that is targeting HER3 is patritumab deruxtecan. This HER3-targeted ADC is delivering a topoisomerase-1 inhibitor cytotoxic payload to HER3-expressing cancer cells. This agent is currently being evaluated in early phase clinical trials, including studies in non-small cell lung cancer and breast cancer.

A phase 2 trial evaluating this agent in lung cancer called HERTHENA-Lung01, has been reported showing early evidence of efficacy and also giving us insights into the safety profile of this drug. Toxicities from this agent included GI-related side effects such as nausea and vomiting, as well as laboratory abnormalities such as cytopenias and alterations in liver enzymes. Fatigue has also been reported.

In terms of breast cancer, this drug is also being evaluated in hormone receptor-positive metastatic breast cancer. The SOLTI-1805 TOT-HER3 clinical trial evaluated patritumab deruxtecan in patients with hormone receptor-positive HER2-negative metastatic breast cancer. In this study, 30 patients were treated, and clinical responses were noted. The side effect profile included nausea, fatigue, abdominal pain, alopecia, as well as cytopenias. In addition, alterations in liver enzymes were noted, including one grade 3 event.

It may be important for us to evaluate the safety of these agents utilizing a multidisciplinary team approach to managing these side effects profiles. Moreover, it's going to be important for us to follow the patient-reported outcomes from larger-phase clinical trials looking at patritumab deruxtecan or other HER3-targeted ADCs.

In summary, this is a very exciting field as we begin to see ADCs targeting antigens that are outside of HER2 or TROP-2. Looking at drugs like TROP-3, targeted ADCs such as patritumab deruxtecan, we are beginning to see proof of principle efficacy, as well as an early glimpse into the safety profile of these agents.

Thank you so much for your time today. I hope this has been helpful.

Announcer:
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