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Gastrointestinal and Hematologic TEAEs Related to ADC Therapy in Gynecologic Cancers

Announcer:
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Dr. Campos:
This is CME on ReachMD. I'm Dr. Susana Campos.

In this episode, we'll talk about the gastrointestinal and hematological adverse events related to ADC therapy that we're seeing in the clinical trials in gynecological cancer. What we know is there is an unmet clinical need for advanced gynecological cancers simply because of poor outcomes despite advances in treatment. What has emerged is the antibody-drug conjugates.

There are several antibody-drug conjugates that have come into play. One specific antibody-drug conjugate is that of trastuzumab-DXd. This was studied in the DESTINY-PanTumor trial. It's important to mention that this agent is approved in advanced breast, lung, and gastric cancer.

The mechanism of action of trastuzumab deruxtecan is an antibody-drug conjugate that consists of a humanized monoclonal antibody covalently linked to a topoisomerase inhibitor, deruxtecan. It's attached to an antibody by a peptide linker. After the trastuzumab deruxtecan binds to HER2, which is found in the malignant cells, it is internalized, and the linker cleavage occurs through various actions of lysosomal enzymes. After it is released through cleavage, trastuzumab-DXd causes targeted DNA damage and apoptosis in cancer cells.

This particular agent was studied in gynecological malignancies. It was studied in endometrial, ovarian, as well as cervical cancer. In each of these 3 disciplines, the overall response rates were greater than that of 50%.

Safety findings from these trials were consistent with the established profile of trastuzumab-DXd. Most common adverse events occurring in greater than 10% of patients consisted mainly of gastrointestinal and hematological events. The gastrointestinal side effects included nausea, diarrhea, vomiting, and decreased appetite. In terms of hematological toxicity, anemia, neutropenia, thrombocytopenia, and fatigue were noted. Grade 3 toxicities were most commonly neutropenia as well as anemia.

In terms of other ADCs, R-DXd [raludotatug deruxtecan] has also been studied in ovarian cancer in a phase 1 clinical study presented by Dr. Katie Moore at ESMO. It's a very interesting ADC. It showed an objective response rate on the order of 46%. In terms of side effects, gastrointestinal side effects were the most common with all-grade adverse events, namely nausea, vomiting, and diarrhea.

So let's discuss what the management protocols for these side effects are. In terms of gastrointestinal, namely nausea and vomiting, if one is dealing with delayed-onset emesis, single-agent, 5-HT_3 RA or dexamethasone can be offered on day 2 and 3 after standard prophylactic regimen administered on day 1. Aprepitant with or without dexamethasone can also be employed if the NK1 has been administered on day 1. If the patient is having early onset diarrhea, an atropine-like compound can be utilized. If the patient is having late-onset diarrhea, loperamide can also be utilized in this setting.

Now let's look at hematological toxicity, neutropenia. G-CSF can be used for those patients at high risk for febrile neutropenia. Additionally, an ADC dose reduction can also occur if the AEs develop. Antibiotics are utilized if the ANC is less than 100 or if the patient has a temperature that is greater than or equal to 38. No dose adjustments for grade 2 or less are made.

In terms of anemia, if the patient experiences a grade 3 to 4, you withhold treatment until this is resolved to less than grade 2; it can resume at a lower dose at that point in time. Oftentimes, we utilize red blood cell transfusions for grade 4 or if patients are symptomatic. It's important to also check for iron studies to make sure that the person is not iron deficient.

In terms of thrombocytopenia, if the patient experiences grade 2 or 3, we usually withhold treatment until the patient recovers to a grade 1 or less. If the patient has a grade 4 toxicity, we withhold and restart at a reduced dose. If a patient has a grade 3 to 4 toxicity in advanced disease, and if there's no recovery to a grade 1 within 42 days, it is recommended that the patient discontinue treatment. Additionally, platelet transfusions can be utilized if the patient is bleeding or in the event to try to prevent bleeding. If there's a poor response to transfusion, then oftentimes we consult with our hematological discipline.

Well, this has been brief but a great discussion. Unfortunately, our time is up, and thank you for tuning in.

Announcer:
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