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Managing Pulmonary and Cardiac Adverse Events Related to ADC Therapy in Breast Cancer

Announcer:
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Dr. Harbeck:
Hello, this is CME on ReachMD, and I'm Dr. Nadia Harbeck. Today, I'll review cardiac and pulmonary adverse events related to antibody-drug conjugate therapies [ADCs] and management strategies for these toxicities. Let's get started.

As you all know, antibody-drug conjugates consist of antibodies with a specific target and a chemotherapy payload. With anti-HER2 antibodies, there may be an association with cardiotoxicity, like we know from trastuzumab. We know with ADCs, the incident is very low. And we know from trastuzumab that this is reversible.

The common payloads are deruxtecan, which is a payload called exatecan, which is a structural analog of a topoisomerase-I inhibitor. The other antibody-drug conjugate that we use in breast cancer in daily clinical practice is sacituzumab govitecan, which has a payload SN-38, which is a metabolite of irinotecan. So the toxicities can be both related to the antibody itself, but mostly to the chemotherapy payload.

Regarding cardiac toxicities, for T-DM1, which is our oldest antibody-drug conjugate used in breast cancer, it is a trastuzumab antibody with emtansine as a chemotherapy payload, has a very low risk of cardiotoxicities. There is some grade 3 and higher hypertension, about 2%, and decreased ejection fractions were mentioned in 1.2% of the patients in the registration trials.

With regard to the newer third-generation ADCs like T-DXd, there is reports of mild decrease in left ventricular ejection fraction, but nothing to be worried about. And sacituzumab govitecan, there is no reports of cardio treatment-related adverse events.

With regard to pulmonary adverse events, they're mostly seen with T-DXd. We do have pneumonitis, interstitial lung disease [ILD], with T-DXd. It occurs in around 12% to 15% of the patients. They're mostly mild, but there could be also some grade 5 toxicities which we unfortunately saw in some of the registration trials. There were 4 deaths in the DESTINY-Breast01 trial. And in DESTINY-Breast03 trial, the ILD was mostly mild, grade 1 or 2. The risk seems to decrease after 12 months of treatment, and it does not appear, and I think this is clinically important and really good information, to be related to the cumulative dose of T-DXd. There is a boxed warning advising healthcare professionals about the risk of interstitial lung disease and embryo-fetal toxicity.

Pulmonary side effects, ILD, are very rare with T-DM1 and sacituzumab govitecan. There's a higher incidence reported with T-DM1, about 2.5% of the patients, again, mild grades, and some reports of ILD if radiotherapy is given concomitantly with T-DM1.

Let's talk about how we manage these ADC-related cardiac and pulmonary adverse events. I think the main message here is interdisciplinary consultations right from the beginning are key. We need to know whom we need to talk to if we have these specific side effects and cannot manage them by ourselves anymore.

We manage the cardiac adverse events according to our guidelines. We have a lot of experience with baseline assessment of cardiovascular toxicity risk factors with an EKG, an echocardiogram, which we do for patients under chemotherapy, which we do for patients under anti-HER2-directed therapies. And so we would follow the same regulations.

For ILD/pneumonitis, I think proactive management and monitoring is crucial. Patient education is also very important. We should have a baseline high-resolution CT and then again every 9 to 12 weeks during treatment. And if there is ILD or pneumonitis suspected, we should follow up very closely according to symptoms and severity of the ILD. We should talk to a pulmonologist early enough if we suspect ILD or pneumonitis for more monitoring and treatment recommendations and be very proactive about steroid use. Steroids are recommended from grade 2 onwards, but we should also consider them for grade 1. And we should, for the time being, discontinue T-DXd for grades 2 or greater. I think that is very important. Grade 1 we can only detect if we have a CT scan, for example, to look for treatment efficacy and we have asymptomatic ILD. Everything that we do because the patient becomes symptomatic will be grade 2 onwards, and we cannot continue with T-DXd according to current recommendations.

For the ILD aspect, it's important, like for all the other toxicities, to collaborate with the multidisciplinary team to educate patients and their other caregivers, be it the family physician, in our country it would also be the practicing gynecologist, about these potential adverse events. And don't forget, there's useful patient information brochures provided by the drug manufacturers.

Thank you for listening. I hope this discussion will be helpful in your clinical practice.

Announcer:
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