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What Do Patients/Caregivers Need To Know About ADCs in Metastatic TNBC?

Announcer:
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Dr. Tolaney:
My name is Sara Tolaney. I'm a Breast Medical Oncologist at Dana Farber Cancer Institute. And today we're going to be highlighting some of the things both patients and providers need to know about antibody drug conjugates when treating patients with metastatic triple-negative breast cancer.

So we do have two ADCs that are available for patients with metastatic triple-negative disease, trastuzumab deruxtecan, as well as sacituzumab govitecan. These ADCs are both highly effective antibody drug conjugates that are FDA approved but they do have different toxicity profiles, and that does need to be kept in mind when treating patients. For T-DXd, one of the toxicities that is known is nausea. And so it is really critical to give antiemetic prophylaxis usually with a three-drug combination. So usually, we are combining dexamethasone with the 5-HT3 receptor antagonist, as well as an NK-1 receptor antagonist. This does usually work very well for premedication. The agent is given once I.V. every 3 weeks and usually treated until someone either has progression or develops toxicity. And one can dose-modify this agent to help treat some of the side effects that emerge. And I find it is quite effective for things like fatigue.

Key side effects that one needs to be aware of outside of just the nausea issue is risk of interstitial lung disease, as well as the lowering of blood counts and potential impact on ejection fraction. For sacituzumab, it is also important to give antiemetic prophylaxis but here I usually give two-drug prophylaxis as opposed to three-drug prophylaxis. The agent is given weekly, 2 weeks on, 1 week off, intravenously. And the toxicities to be aware of do include neutropenia, nausea, diarrhea, and alopecia. So very important to be aware of these.

I think you can see these data a bit more granularly when looking at the T-DXd data, where again, the most common toxicity really is nausea. I think we're not used to thinking about neutropenia with HER2-directed ADCs since we've previously been used to T-DM1 which does not cause neutropenia, but this agent, T-DXd, does. And then again with the ILD, it is really important to be aware of because it is 12% of patients who can experience ILD, and unfortunately, can even lead to death and a small number of patients. And so that has been quite critical to be aware of. That was not the case in D-B04, but has been seen in other studies.

I think the other thing to be aware of is most of the ILD is low grade. And so you know, again, you can have people who have asymptomatic ILD, and so monitoring this with routine scans is really pretty critical to be able to catch that ILD. And then it's really important to hold the drug at onset of ILD and discontinue it if they have symptomatic ILD.

We talked about the issues with nausea with T-DXd. And again, remember the three-drug prophylaxis is very effective. For the interstitial lung disease, generally, I do like to scan patients every 6 to 9 weeks to make sure that I'm monitoring them carefully. If they have asymptomatic ILD, I do hold drug. I usually do give steroids. It's not required, but I tend to hold until it resolves completely on imaging and then I re-expose them. If it's been less than 28 days, I continue at the same dose. If it's been longer than 28 days, I do dose-

modify. But grade 2 and higher ILD, you have to discontinue drug. You cannot re-expose them to T-DXd, and you do treat with steroids.

For sacituzumab, just be very aware of the neutropenia because a lot of patients, do you require growth factor support for this agent. And so please do introduce that if patients are experiencing neutropenia. Provide patients with loperamide as needed for the diarrhea, and do counsel patients about risk of developing alopecia with this agent.

Again, we did talk about neutropenia for both of these ADCs, and growth factor support can be quite helpful. With sacituzumab, growth factor is a little more complicated because it's a day 1 and 8 drug, so one could choose to use a long-acting growth factor after day 8, or to use short-acting growth factor after day 1 and long-acting after day 8. And it really depends on when the neutropenia is arising. And really, again, diarrhea is pretty mild with sacituzumab, but do make sure patients do have loperamide on hand.

So I think really just to summarize with both of these ADCs to me, the most critical thing is warning patients about the potential side effects so that they can contact you with any issues right away. And particularly with T-DXd, that ILD is something you do need to discontinue drug if they have symptomatic ILD, and at least hold it for grade 1 asymptomatic ILD because you don't want to run into risks of developing higher-grade toxicity.

Thank you very much for your attention.

Announcer:
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