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Monitoring and Managing Adverse Effects With ADCs in HR+ Breast Cancer: Strategies To Improve Outcomes

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Mayer:
Hello, I'm Erica Mayer from Dana Farber Cancer Institute. And I'd like to discuss monitoring and managing adverse effects with antibody drug conjugates in hormone receptor positive-breast cancer.

We have two exciting new antibody drug conjugates which have entered our treatment portfolio for advanced disease. First, this includes T-DXd, or trastuzumab deruxtecan, which was studied in the DESTINY-Breast04 study where the use of T-DXd had superior outcomes to treatment provider choice. What we learned from DESTINY-Breast04 is that there are specific side effects that we're seeing with T-DXd. Common side effects include GI toxicity, such as nausea or vomiting, and fatigue and alopecia were also prominent. Notably, there was less hematologic toxicity seen with T-DXd in comparison to the treatment provider choice. The most common adverse effects associated with dose reduction included nausea and fatigue. And with treatment discontinuation, there was interstitial lung disease. Of note, about 12% of patients experienced any-grade interstitial lung disease, and importantly, a small number, 0.8%, experienced grade 5 or fatal interstitial lung disease. So this is a very important toxicity to be aware of.

Recently, we saw updated toxicity information from DESTINY-Breast04 presented at 2023 ESMO Breast. In this figure, you can see the median time the first onset of toxicity and the median duration of the first event. Importantly, the median time to onset for both GI and hematologic toxicities was generally in the first month of treatment, so we know to watch patients carefully for these side effects as soon as they start therapy. The median duration of the first toxicity event for GI toxicity was fairly short, 3 to 10 days. For hematologic toxicity, this was longer, from about a week to even up to a month.

Importantly, when you look at these figures, you can see that interstitial lung disease had a median time to first onset of about 4 months, 120 days. And this means that this is a side effect that we have to be vigilant for, not only when we start patients on therapy, but continuously for patients on therapy.

This slide shows us ways to both monitor and manage interstitial lung disease with T-DXd. In terms of monitoring, it's very important to make sure that patients are reporting any new pulmonary symptoms that they might experience. And we want to monitor patients closely with CT imaging every 6 weeks to begin therapy. If there's any signs of either radiologic interstitial lung disease and/or symptoms, we want to hold therapy and, certainly in the setting of symptoms, refer to pulmonology for further workup. For grade 1 disease, which is just radiologic findings without symptoms, we want to hold until completely resolved to grade 0. If a patient has grade 2 to 4 interstitial lung disease, meaning it's symptomatic, then unfortunately, they need to permanently discontinue therapy. Patients who have grade 2 or higher disease need to receive steroids, it's more optional for grade 1. And for grade 1, there is the option to rechallenge patients with therapy either at the same dose or at a reduced dose.

We also saw some data recently about what happens when we retreat patients. There were 6 patients in DESTINY-Breast04 who had

grade 1 ILD who were rechallenged with T-DXd. One of those patients experienced ILD again, but at the time of data cut-off, 3 of the 6 patients were still receiving T-DXd. And I think this shows us that we can safely and carefully restart therapy, and patients can gain more benefit from the agent if we can get it back on board.

Nausea/vomiting is also a significant side effect with T-DXd. We want to premedicate with appropriate antiemetics. We want a patient to take home appropriate antiemetics. And if a patient has significant GI toxicity, then we want to think about a dose reduction.

The other main antibody drug conjugate to keep in mind is sacituzumab, which was studied for hormone receptor-positive disease in the TROPiCS-02 study. In this study, the major side effects that we're seeing included hematologic, such as neutropenia, diarrhea, alopecia, and fatigue, although thankfully rates of febrile neutropenia were low.

Patients who are receiving sacituzumab need to be educated about the possibility of diarrhea, and need to have anti-diarrheals available and to use them in the setting of any new diarrhea. A dose reduction may be necessary if the patient experiences significant diarrhea.

Additionally, we want to monitor and manage neutropenia, particularly for sacituzumab. Patients have to have an ANC of at least 1500 on day 1 of each cycle, or at least 1000 on day 8. If a patient experiences neutropenia, we should use growth factor support, either short-acting, or we can even give long-acting support on day 9 of each cycle. This is a strategy that works very well.

Thank you very much for listening and I hope you found this helpful.

Announcer:
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