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Hematologic Adverse Events With ADCs in Breast Cancer: Optimal Management Strategies

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

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Dr. Harbeck:
Hi, this is CME on ReachMD, and I'm Dr. Nadia Harbeck. In this episode, I'll talk about the hematological adverse events related to antibody-drug conjugates and how to manage them.

With regard to ADCs, we have an antibody component and we have a chemotherapy payload, and hematological side effects are mostly caused by the chemotherapy payload.

So what did we see in the clinical trials regarding hematological side effects with ADCs? Neutropenia: With T-DM1, it's very rare. We have all-grade, around 5% to 10% and grade 3 also around 6%. With T-DXd, it's frequent. It was the main reason for dose reductions or drug interruptions with around 70% frequency. And febrile neutropenia, however, is rare. With sacituzumab govitecan, we saw some severe cases, 13% of patients developed a grade 4 event, and febrile neutropenia was seen in 6%. There's a boxed warning for neutropenia and diarrhea.

With regard to anemia, with T-DM1, it's low, around 1% to 3%; T-DXd D, grade 3 or 4 around 10%; and sacituzumab govitecan around 8%.

Thrombocytopenia, with T-DM1, it's a common adverse event, about 48% of the patients, and grade 3 and higher seen in about 12% of the patients. Usually developed fast, during the first 2 cycles of treatment. There was some epistaxis in around a third of the patients but no severe hemorrhagic events. And the incidence seems to be a little bit higher in the Asian population. With T-DXd, there's about 7% grade 3 or 4 thrombocytopenia, and with sacituzumab govitecan, around 3%.

So with regard to neutropenia, we should always keep in mind that we can use G-CSF short or long acting, also depending on the cycle and the severity of the event. And we should have a dose reduction according to the package insert if there is more adverse events than just asymptomatic lower-grade neutropenias. We don't need to do dose adjustments for events that are grade 3 or lower. And for sacituzumab, if the neutropenia occurs on day 1, we should have a short-acting G-CSF during the first week, days 4 to 6 on the treatment cycle. And if there is neutropenia on day 8, then a long-acting pegylated G-CSF would be a good option. And we always give that on the day after the infusion.

With regard to anemia grade 3 or 4, we should hold the treatment until it's resolved and then resume at a lower dose level. We can give red blood cell transfusions if it's grade 4 or symptomatic grade 3. And for lower-grade anemia, we could also look at the iron levels and start iron supplementation.

Thrombocytopenia, we should hold the treatment if it's grade 2 or 3 until the thrombocytes have recovered to grade 1. And with grade 4, we should stop the treatment and restart it and reduce dose. We should also think about whether it's advanced disease or early disease. And if there's an advanced disease, no recovery within 42 days, discontinue treatment. Platelet transfusions should only be used if

there's bleeding or to prevent bleeding if the platelets are really low. And if there's a poor response to the transfusion, we should talk to our hematological colleagues.

Again, with all of these side effects, it's always important to see that we're working in a multidisciplinary team, talk to our patients, and educate also their other caregivers, and if we have access to them, use the resources that are provided by the manufacturer.

So in summary, I think it's key to be aware of these potential hematological toxicities. We usually don't connect antibodies with them, but in this case, antibody-drug conjugates are probably more like chemotherapy components. We should monitor them and use G-CSF prophylaxis if the regular intervals cannot be maintained or symptomatic events happen.

Thank you for listening. Please tune in to the other episodes for discussion on other ADC-related toxicities and best practice how to manage them.

Announcer:
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