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https://reachmd.com/programs/cme/how-can-you-recognize-and-manage-the-common-adverse-events-seen-with-adcs/14293/

Released: 06/15/2022
Valid until: 06/30/2023
Time needed to complete: 1h 21m

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How Can You Recognize and Manage the Common Adverse Events Seen With ADCs?

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum.
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Dr. Kalinksy:
Hi, this is Kevin Kalinsky. I'm the Glenn Family Breast Cancer Center director at Winship Cancer Institute in Atlanta, Georgia. I'll be talking about how you can recognize and manage the common adverse events seen with anantibody-drugonjugates.

From the ASCENT trial, we saw significant benefit when comparing Sacituzumab Govitecan versus physician choice chemotherapy in patients with triple-negative breast cancer who had tumors that had progressed on at least two lines of therapy in the advanced setting, and if patients had progression within the operable setting within a 12 month period, that counted as a line. And you can see that there was a statistically significant improvement in overall survival comparing Sacituzumab Govitecan versus physician choice chemotherapy with a hazard ratio of 0.48: the statistically significant P value.

When looking at the treatment-related adverse events, so these were the all-grade events from the ASCEND trial that were greater than 20% or for those grade 3/4 events that were at least 5% of the patients. The main toxicities that we see, especially comparing Sacituzumab Govitecan versus physician's choice therapy is neutropenia, also diarrhea. We can also see numerically a higher rate of other heme toxicities like leukopenia and febrile neutropenia. It's also worth noting that GCSF usage was higher in ASCENT for the Sacituzumab arm at 49% compared to physician choice chemotherapy at 23%, though the dose reduction rates were similar due to treatment-related adverse events. It is also worth highlighting that there is a risk for diarrhea, nausea, fatigue, and alopecia. I know it says 46% here, but all of my patients have lost their hair with Sacituzumab Govitecan. The other thing just to highlight is that there is no neuropathy or interstitial lung disease that has been reported with Sacituzumab Govitecan.

So, we showed data at ASCO in 2021 that was just comparing the safety in the patients in the ASCENT trial who were over than or equal to 65 years of age. And overall the toxicity profile was similar. When you're comparing physician choice chemotherapy to Sacituzumab Govitecan, numerically the same things were seen where there's a higher rate of neutropenia and leukopenia, diarrhea, and also febrile neutropenia. Also, in the elderly population, 53% of patients required a GCSF usage and then 65% used anti-propulsives to manage their gastrointestinal issues.

You can see that we're talking about the TROPION study, which is discussing a different trope to antibody drug conjugate, this one from a different company which is given once every three weeks. And from this phase one study, we had some information just about initial activity and triple negative breast cancer as well as some safety data.

And you can see the treatment-emergent adverse events in 15% of the patients or greater and see that the toxicities are a little bit different with this agent where, yes, you can have nausea, but there's actually a higher rate of stomatitis, predominantly grade one or two again, again no ILD, and there's a low frequency of hematologic toxicity, as well as diarrhea.

If you look at the next slide, you can see the discussion about HER2-Low breast cancer at ASCO this year at the plenary session, Dr.

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Moody's gonna be reporting the results of the DESTINY-04 study, which has the potential for being a practice-changing trial, and this slide here is just showing the rates of having HER2-Low, which is IHC 1+ or 2+ with a negative immuno situ hybridization. And you can see that there's a rate in the hormone receptor positive population, this is about 55% and the triple negative population, nearly 40%.

And we've seen toxicity from DESTINY-Breast03 comparing T-DM1 and T-DXd, where T-DXd really was significantly improved, and these data have been published in the New England Journal of Medicine.

And if you move to the next slide, you can see the AEs of special interest, in particular drug-related interstitial lung disease, or pneumonitis. And one of the things that we learned from the development of this drug early on was to keep a close eye on this potential toxicity, because there were some patients in the early study which had some deaths related to ILD. So now, I think there has been clear messaging that if a patient has a grade 2 or higher ILD, one should stop the drug and not re-challenge. And these data from this randomized study have demonstrated that, in fact, this has been clearly messaged where there are no grade 4 or 5 adjudicated drug-related ILD events with T-DXd and we'll see in DESTINY-04 what the toxicity profile looks like as well as the activity. I really just wanted to present these data because there is a high chance that these could be practice-changing after we see the data presented at ASCO.

So, that's a summary of the events that we can see with some of the antibody drug conjugates. Hopefully it's been clear that not all antibody drug conjugates are the same. For instance, we see with the different trope 2 antibody drug conjugates Sacituzumab Govitecan is the only one that's currently approved, but we see with the other trope 2 antibody drug conjugate that you can have stomatitis and low rates of gastrointestinal issues. And then, with T-DXd, the main toxicity to be most aware of is, in particular, this interstitial pneumonitis. Thank you for your attention and look forward to other discussions regarding this topic. Thank you.

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