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Managing Adverse Events Associated With TROP2-Directed ADCs in Metastatic TNBC

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Dr. Traina:

Welcome. This is CE with GLC. I'm Dr. Tiffany Traina. Today, I'll discuss management strategies for adverse events associated with TROP2-directed antibody-drug conjugates that are used in metastatic triple-negative breast cancer.

So let's get started with TROPION-Breast02. And I think it's important to remember that the antibody-drug conjugate datopotamab deruxtecan was used for twice the duration of treatment time than the chemotherapy arm. And even despite that longer duration of treatment, the rates of grade 3 or greater or serious treatment-related adverse events were similar between the antibody-drug conjugate and chemotherapy. And that is reassuring in that kind of exposure-adjusted analysis.

And also discontinuations of datopotamab due to toxicity were lower, were almost half that of what was seen with chemotherapy.

Also, something quite reassuring is that treatment-related adverse events associated with death did not occur in either study arm—either the datopotamab arm or the chemotherapy arm. So really encouraging toxicity.

Now, there were 3 adverse events of special interest I want to pause on and just spend a moment talking about. One of interest is ILD, because deruxtecan payload is similar to what is in trastuzumab deruxtecan. So some may wonder if ILD rates were a concern. It's quite reassuring to see that ILD was incredibly uncommon, less than 1% grade 3 or greater ILD with datopotamab deruxtecan, and that actually looked quite comparable with chemotherapy.

The other 2 adverse events of interest are oral mucositis or stomatitis and ocular surface events. So oral mucositis occurred about 8% grade 3 or greater, so the vast majority of these events were low grade, grade 1 or grade 2.

When we think about ocular surface events, again, the vast majority of these are grade 1 asymptomatic or grade 2 events. About 7% were grade 3 or greater, and primarily these events are dry eye or keratitis.

There are also prophylactic strategies to manage adverse events, like stomatitis, for example.

Also, for dry eye, I think there are definitely strategies that can be used in collaboration with optometry and ophthalmology for monitoring while patients are on datopotamab.

If we shift gears a bit and think about ASCENT-03 and the use of sacituzumab govitecan, here we also saw fewer treatment-related adverse events that were leading to discontinuation with the antibody-drug conjugate as compared to chemotherapy, fewer needs for dose reductions, comparable dose interruptions between sacituzumab and chemotherapy, and I think there were, unfortunately, some treatment-related deaths on study with sacituzumab, about 6 treatment-related deaths on study with sacituzumab.

Many of these related to infection secondary to neutropenia, and so it's important to remember that this is something we can prophylax against with the use of sacituzumab.

When we think about what were the most common adverse events with sacituzumab as compared to chemotherapy, neutropenia was quite common, nausea, alopecia, and diarrhea probably more common with sacituzumab. And grade 3 diarrhea occurred in about 9% of patients, and we see that consistently across the sacituzumab trials.

When you adjust for exposure, similar to our discussion with datopotamab, patients were on their antibody-drug conjugate much longer than they were on chemotherapy, so those exposure-adjusted analyses and incidence rates show that even despite that, diarrhea did favor chemotherapy more so than sacituzumab, and neutropenia also favored chemotherapy a little bit more so than sacituzumab.

So I would highly recommend that use of prophylaxis to mitigate toxicity, mitigate adverse events, enable our patients to stay on these highly effective treatments that much longer.

So with that, I am out of time. I want to thank you for listening. Thank you for joining us.

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