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Case Application: Adverse Event Management of Patients With EGFRm Resistance Treated With Novel HER3-Directed ADCs

Announcer:

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

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Dr. Yu:

This is CME on ReachMD, and I'm Dr. Helena Yu, a thoracic oncologist at Sloan Kettering in New York.

Dr. Jänne:

And I'm Dr. Pasi Jänne, a thoracic medical oncologist at the Dana Farber Cancer Institute in Boston.

Dr. Yu:

Pasi, let's start our discussion with a case. I have a patient, a 46-year-old woman with EGFR exon 19 deletion-positive lung adenocarcinoma, who initially presented with stage IV disease with metastases to lung, lymph node, brain, and bone. She started treatment with osimertinib, had an excellent partial response to therapy that lasted 16 months, but then subsequently had disease progression with new bone metastases, and then was started on carboplatin-pemetrexed with osimertinib continued. She received 4 cycles of carboplatin-pemetrexed, followed by 4 cycles of pemetrexed maintenance, until she had evidence of progression of disease with growing lung nodules as well as new liver metastases.

She then started HER3-DXd, patritumab deruxtecan, on a clinical trial. The first cycle went well. She had no problems during the infusion but did have some nausea that limited food and liquid intake. So I think, first, would there be medications, or premedications that you would use to help with nausea in this case?

Dr. Jänne:

What we found is that using premedications such as 5-HT3 antagonists, like ondansetron, has worked well for patients as well as corticosteroids such as prednisone and dexamethasone. And finally, olanzapine, we found it to be useful as a premedication for patients who get severe nausea from chemotherapy-like medications like HER3-DXd. And with appropriate premedication, we've definitely seen a reduction in the severity of nausea or, in some cases, no nausea at all, which has been helpful for patients being able to maintain oral intake.

Dr. Yu:

Yeah, absolutely. I think that the medications with the infusion and then the dexamethasone also just really help. And I think remembering that these have a chemotherapy component and so using the similar premeds that we use with, say, platinum-based chemotherapy makes sense.

So this patient, she presented for Cycle 2, Day 1, ready to get her second infusion, but upon blood work, we saw that her total white count was 2.0, her ANC was 0.9, platelets were 95, and hemoglobin was 12.7. And so in that situation, Pasi, would you proceed with treatment, or would you intervene in some way? And what could be done to prevent this in the future?

Dr. Jänne:

I think in this situation, I'd probably delay her treatment a little bit just to give the bone marrow a chance to recover a little bit more. We do know that hematologic toxicity is seen with HER3-DXd, and here we have both neutropenia and a little bit of thrombocytopenia. And to prevent this in the future, we'd probably administer growth factor support after the infusion with a long-acting G-CSF to prevent neutropenia from happening.

Dr. Yu:

Yeah, I agree. I think one thing to note is, in the clinical trials, these cytopenias weren't associated with any kind of clinical complications like bleeding or neutropenic fever, and they do seem to be front-loaded with the first few cycles. And certainly both the nausea and the cytopenias, if persistent, would respond to a dose reduction of HER3-DXd. So I think those are different ways to help mitigate these issues.

With that, our time is up. We hope you found this quick case review helpful, and thanks so much for listening.

Announcer:

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