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Distinguishing First-Line Treatment Adverse Event Profiles in HER2-Negative Upper GI Cancers

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Dr. Cleary:
This is CE on ReachMD, and I'm Dr. James Cleary. In this episode, let's turn to the adverse event profiles of regimens that are given in HER2-negative gastroesophageal cancer.

The first regimen I wanted to cover is zolbetuximab. Again, zolbetuximab was recently approved by the FDA for tumors, for gastroesophageal cancers that are claudin 18.2 positive. So for patients who have a claudin 18.2 positive, the FDA has approved the use of zolbetuximab with 5-FU and platinum-based chemotherapy.

The issue with zolbetuximab, and the reason it's important to talk about this is, unlike antibodies that, as oncologists, we've gotten used to using, this one causes nausea. So it really can cause chemotherapy-like nausea, and it hasn't really been on people's radar screens. So really the main teaching point here is, please, when you're giving zolbetuximab, please know that this is going to make the nausea from the FOLFOX significantly worse. But there are ways to manage this. And you might be wondering why is that; so typically antibodies, like EGFR antibodies, they might cause a rash, but it's not going to cause nausea. The reason zolbetuximab is causing nausea is claudin 18.2 is actually expressed on normal gastric epithelium. And so when the zolbetuximab binds to the claudin 18.2 in the normal gastric cells, it's causing irritation, making patients nauseous.

Ways to counteract this—I like to give several pre-meds with the FOLFOX/zolbetuximab, really, just to try and make this much more tolerable for the patients. So the regimen I give, I like to give an NK-1 antagonist, like Emend, we use Cinvanti in my institution, which is a long-acting NK-1 antagonist. I also like to give a long-acting 5-HT3 antagonist. I typically give Aloxi and I also give dexamethasone. So again, for pre-meds, before you give this FOLFOX/zolbetuximab, I like to give a long-acting like Emend, a long-acting 5-HT3 inhibitor, like Aloxi and Decadron.

In addition, though, for nausea that persists despite all those pre-meds, we found that olanzapine is very helpful. So please have a low threshold to using olanzapine 5 or 10 mg that the patients can take nightly.

So in terms of the toxicity profile for the PD-1 antibody chemotherapy regimens, the toxicities—obviously, you got chemotherapy toxicities from the FOLFOX like myelosuppression, nausea, neuropathy. But from the PD-1 antibody, those can cause autoimmune toxicities such as autoimmune pneumonitis, hepatitis, and colitis.

If patients get a significant autoimmune toxicity, such as severe diarrhea, shortness of breath, or autoimmune hepatitis, those patients

need to be hospitalized and be put on high doses of IV steroids. Many times, I'll actually consult with a specialist, whether it's a pulmonologist if the person has autoimmune pneumonitis, or a gastroenterologist if they have autoimmune colitis.

Subcutaneous nivolumab has shown similar efficacy to IV nivolumab. And really the selling point for subcutaneous nivolumab is convenience, that it can be given in as short a time as 5 minutes.

Thank you.

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