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<https://reachmd.com/programs/cme/pivotal-data-in-anti-pd-1-strategies-for-her2-negative-upper-gi-cancers/37690/>

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Pivotal Data in Anti-PD-1 Strategies for HER2-Negative Upper GI Cancers

Announcer:

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Dr. Cleary

This is CE on ReachMD, and I'm Dr. James Cleary. The current standard of care for most HER2-negative gastroesophageal cancers involves anti-PD-1 therapy in combination with chemotherapy. The treatment landscape, though, has changed dramatically over the past few years, with the emergence of immunotherapy as well as targeted therapy to claudin 18.2. And this has really impacted our first-line treatment options for patients with gastroesophageal cancer. Let's review the pivotal data that led to the approval of anti-PD-1 antibodies in combination with 5-FU and platinum-based chemotherapy.

There are three anti-PD-1 antibodies that are approved as first-line therapy in metastatic gastroesophageal cancer: nivolumab, pembrolizumab, and tislelizumab.

What gives me a lot of confidence about using these agents is the trials from these three different PD-1 antibodies had very similar and, in many ways, consistent results. And that really gives me confidence that PD-1 immunotherapy really does enhance the efficacy of 5-FU and platinum-based chemotherapy in patients with PD-L1 positive gastroesophageal cancers.

In looking at the trials, the results of the trials actually were very similar. So in the PD-L1 positive population—and again, this means that patients who had a tumor with a PD-L1 CPS score of 1 or greater—although I should note in the tislelizumab trials, they used the TAP PD-L1 scoring system rather than CPS. But in PD-L1 positive tumors, the addition of the PD-L1 antibody to 5-FU and platinum-based chemotherapy in the CheckMate 649 trial, improved overall survival. Similarly, the addition of pembrolizumab to 5-FU and platinum-based chemotherapy in the KEYNOTE-859 trial improved overall survival. And then in the RATIONALE 305 study, the addition of tislelizumab to FOLFOX or CAPOX improved overall survival.

So again, the results of all 3 of these agents, all 3 trials that led to the FDA approval of these anti-PD-1 antibodies, were very, very similar. And also which gives me confidence as a clinician in using these is all 3 of these regimens have been well tolerated. I think, over the past 5 to 10 years, medical oncology has really gotten a lot of experience using checkpoint inhibitor therapy. We know the side effects of these regimens, things like autoimmune pneumonitis, colitis, and hepatitis and we've gotten used to using them.

Recently, nivolumab was approved by the FDA to be given as a subcutaneous injection. So now the FDA allows us to give nivolumab either as IV or sub-Q. One possible advantage of giving it sub-Q is logistically, it's just easier for the patients. And so if you have a patient, especially a patient who's getting single-agent nivolumab, you're really going to save them a lot of time and also some infusion room space by using the nivolumab sub-Q agent.

So really, when I think about these three regimens of giving 5-FU-based chemotherapy with platinum-based chemotherapy with either nivolumab, pembrolizumab, or tislelizumab, I think the efficacy of all three regimens is similar, and the side effect of all three regimens is similar.

It's really important to point out, though, that there was a meeting held by the FDA just to harmonize the definitions of when we're going to use these regimens about a year ago. And what this meeting at the FDA showed is, previously, nivolumab had an FDA approval even for patients with gastroesophageal cancer that had PD-L1 negative tumors. Now, that FDA approval has changed, and the FDA approval is only for patients who have a gastroesophageal cancer that's PD-L1 positive.

So really, I think the big teaching point here is when you have a patient with metastatic gastroesophageal cancer, you can give an anti-PD-1 antibody, as long as the tumor is PD-L1 positive.

Thank you.

Announcer:

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