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Tailoring First-Line Regimens: Patient-Centric Selection in Metastatic ESCC

Dr. Yoon:
This is CME on ReachMD, and I'm Dr. Yoon. And in this episode, I'll be discussing a patient case example on first-line treatment selection for metastatic esophageal squamous cancer.

So, my patient is a 50-year-old gentleman, former smoker, presented with dysphagia. This is the standard presentation. EGD identified a mass in the proximal esophagus above the carina, which was biopsy confirmed to be squamous cancer. And the fact that the mass is above the carina is what makes surgical resection challenging. So the CAT scan of the chest, abdomen, pelvis and PET/CT showed positive nodes in the supraclavicular region, as well as in the lower retroperitoneum at the level of the renal vessels. So for me, the renal vessels is a definite demarcation, at which point it's generally not surgically resectable. So, the fact that there are positive nodes in the lower retroperitoneum is what makes this stage IV. The patient is able to drink liquids, but is having difficulty with solids and ingesting perhaps 1200 calories per day, which means that we, so-called, need a response, and that usually means cytotoxic therapy, and he has a good performance status.

So, by the time I see the patient, we don't typically have the PD-L1 status. And if we don't, I would still generally start with FOLFOX plus immunotherapy. And I start with empiric immunotherapy in esophageal squamous cancer compared with adenocarcinoma, because squamous patients seem to be more likely to be PD-L1-positive and generally seem to benefit more from immunotherapy than the adenocarcinomas. So then if the PD-L1 CPS returns less than 1, I would consider removing the immunotherapy, and this is consistent with the recent ODAC recommendations.

Now, if the treatment options in the first-line setting are expanded with an FDA approval of tislelizumab, that could impact treatment selection in certain situations. Tislelizumab is the only immunotherapy in this indication based on a global phase 3, where the trial design allowed for use of a chemotherapy backbone other than platinum/fluoropyrimidine. And half the patients in the tislelizumab phase 3, which was RATIONALE-306, received cisplatin plus paclitaxel. And this group benefited just as much as the cisplatin/fluoropyrimidine group. So, the most evidence-based option would be to offer tislelizumab in patients where I would offer platinum/ paclitaxel backbone chemotherapy instead of FOLFOX.

So some situations to consider avoiding FOLFOX are patients who prefer every-3-week dosing, with the caveat that nivolumab/pembrolizumab are also available every 6 weeks, so that still is an option. But another situation is patients who might wish to avoid a 46-hour pump, because the paclitaxel dosing doesn't require that, and it's given every 3 weeks. And this can make an effect on patients in terms of how often they come back.

Another situation are patients who have a DPYD deficiency. Specifically, they might be homozygous or have compound heterozygosity. And some patients in the country are now implementing DPYD screening in some form. It's not very common, but it's somewhere less than 1% of the cancer population.

Another group where we might want to consider avoiding FOLFOX chemotherapy are patients who develop an oxaliplatin reaction. And this doesn't usually happen on the first dose, but after a few doses. We could give a desensitization protocol for oxaliplatin, but this can be onerous for the patient, as well as taxing for the system. And so that might be a situation where switching to taxane could make

sense.

So that concludes this case review in the first-line treatment of esophageal squamous cancer. Thanks for listening.