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## The Impact of First-Line Treatment on Subsequent Treatment Options for Metastatic ESCC

### Dr. Yoon:

This is CME on ReachMD, and I'm Dr. Yoon. In this episode, I'll be discussing patient case examples on the impact of first-line treatment, or adjuvant treatment, on subsequent treatment options for patients with metastatic esophageal squamous cancer.

So let's think about 3 different scenarios. The first scenario is a patient with advanced esophageal squamous cancer who received chemotherapy plus immunotherapy in the first-line setting, and then had disease progression. So typically, in this situation as second-line therapy, I would proceed with chemotherapy alone, without immunotherapy, off-protocol that is. And the specific second-line chemotherapy regimen that I would prefer would depend on which regimen was given in the first-line setting. So if in the first-line setting, the regimen was FOLFOX plus immunotherapy, then second-line options that I would typically consider would be FOLFIRI if the patient has a good performance status, or irinotecan or a taxane if the patient's performance status were not as good. I personally don't have a strong preference of one regimen over another, and the precise choice depends on the side effect profile and schedule, and that's usually discussed and sort of negotiated the pros and cons with the patient.

So now let's consider a different patient. Now, this is a patient who, for whatever reason, did not receive immunotherapy in the first-line setting. Then in that situation, in the second-line setting, I would favor the use of immunotherapy if possible. And there are three immunotherapy agents that are approved in this indication, and they are tislelizumab, nivolumab, and pembrolizumab. And here, the role of the PD-L1 biomarker is a little less clear than it is in the first-line setting, in my opinion, and compared with adenocarcinomas in the first-line setting, because there's less data. Certainly, if the PD-L1 CPS is 10 or higher, I think any of the approved immunotherapy agents would be fine. And for most patients with a CPS 1 or higher, I would offer immunotherapy. And the agents in this setting are tislelizumab and nivolumab.

Now finally, there's the third scenario, the patient who progresses on adjuvant nivolumab after trimodality therapy. This is a fairly uncommon situation, because many esophageal squamous patients undergo chemoradiation, whereas, in my experience, relatively few undergo trimodality therapy, which would be chemotherapy plus radiation, followed by surgery. And in that situation, after trimodality therapy, adjuvant nivolumab is an option based on the CheckMate 577 data. So now if you have a patient who did undergo trimodality therapy, and then the patient started adjuvant nivolumab, and then the patient's tumor recurs while on adjuvant nivolumab, then in that situation, I would give chemotherapy alone. And right now, there are currently no data to support continuation of immunotherapy after progression on immunotherapy.

Now, having said that, if the PD-L1 CPS were 10 or higher, or the TPS were at least a 1, and this patient was on adjuvant nivolumab and had been on it, particularly for a while, then I would actually consider continuing immunotherapy and combining immunotherapy with a chemotherapy regimen, preferably a chemo regimen that was different than the one given during combined modality treatment.

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