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Released: 03/31/2025
Valid until: 03/31/2026
Time needed to complete: 46m

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Distinguishing Between Anti-PD-1 Agents in ESCC Combination Therapies

Announcer:
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Dr. Ajani:
Hello, everyone. This is CME on ReachMD, and I'm Jaffer Ajani. I'm a GI medical oncologist working at MD Anderson Cancer Center. Today, we're going to dive right into a discussion about anti-PD-1 agents in esophageal squamous cell carcinoma and their distinguishing features.

So I'd like to start out by talking about the tumor microenvironment for squamous cell carcinoma. And squamous cell carcinoma, in molecular profiling, is very similar to head and neck cancers. So head and neck cancers, as you well know, can be caused by smoking and drinking. Similarly, squamous cell carcinoma, the carcinogenic factors are predominantly smoking and drinking that causes a lot of damage to the primary tissue, the squamous epithelium of the esophagus. And so there's an inflammatory component to that, which can be distinguished with adenocarcinoma, where inflammation does play a part, but the level of inflammation is different. So a squamous cell carcinoma, just like head and neck cancers, are clearly more responsive to immune modulation, as opposed to only some patients in adenocarcinoma.

So the role of immunotherapy seems to be very important squamous cell carcinoma of the esophagus. And more patients tend to benefit. One clear example is 91% of esophageal squamous cell carcinoma are PD-L1-positive, as opposed to 65 to 70% of adenocarcinoma.

So next, I would like to mention about distinguishing features among PD-1 inhibitors, and particularly those that are being used in the context of squamous cell carcinoma of the esophagus.

So the pre-clinical characteristics are somewhat different. Now, we start with tislelizumab, which is an anti-PD inhibitor, and it is a humanized antibody with a low risk of infusion reactions, and it has a very high affinity for PD-1 inhibitor, as compared to nivolumab or pembrolizumab. So give you one example, tislelizumab can bind to PD-1 receptor covering about 80% of the area where PD-L1 or PD-L2 will bind, so it will inhibit PD-L1 and PD-L1/2 compared to nivolumab and pembrolizumab, both of those will inhibit PD-L1.

In addition to the high affinity means, the binding to the receptor is very tight, and this leads to slower detachment from the receptor. So once you bind the PD-1 receptor, what can happen is the T cells, particularly killer T cells, CD8 cells, can proliferate and migrate and start killing the cancer cells. So if you can allow the T cells to proliferate for longer time and allow killing of cancer cells, that can produce an advantage that other drugs may not have. So the detachment of tislelizumab from the PD-1 receptor is very slow, so it remains bound to the receptor for a longer time compared to nivolumab or pembrolizumab.

The other distinguishing feature of tislelizumab from nivolumab or pembrolizumab, is that the FC portion of the antibody has been modified so that it doesn't bind to the macrophages. And if you can inhibit binding of macrophages, you basically avoid resistance to

PD-1 inhibitor. So that's a very unique feature of tislelizumab. Whether such preclinical advantages can truly manifest in the clinical setting is not completely known, but it certainly makes it an attractive drug.

In addition to that, we also know that it has less side effects compared to the two other anti-PD-1 molecules such as nivolumab or pembrolizumab.

Well, now our time is up, and thank you so much for participating in this program.

Announcer:
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