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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Risk Stratification and Patient Selection for Perioperative ICIs

Announcer:
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Dr. Adkins:
This is CE on ReachMD, and I'm Dr. Douglas Adkins. In this brief lecture, I will discuss risk stratification and patient selection for perioperative immune checkpoint inhibitors in locally advanced head and neck squamous cell carcinoma.

Most patients with head and neck cancer present with locally advanced disease, and the most common primary tumor site is that of the oral cavity, reflecting 60% of cases, followed by larynx, oropharynx, and hypopharynx.

It is important to consider both adverse clinical and pathologic features in determining appropriate treatment pathways for these patients. I've listed here adverse clinical features, which include higher T stage, a smoking history, and primary tumor site involving hypopharynx and oropharynx. These features carry a poorer prognosis.

In the pathology arena, high-risk pathology is well recognized as an adverse prognostic feature for local or regional recurrence. This is defined by positive margin and/or extranodal extension.

A large majority of patients, however, will have intermediate-risk pathology; that is, it includes lymphovascular or perineural invasion, 2 or more positive nodes, a single node more than 3 cm, or T3 or N2 disease. And then finally, HPV status, in that HPV-negative tumors carry poorer prognosis.

It's important to consider the cause of cancer in determining appropriate management of these patients. The 2 common causes of head and neck cancer include carcinogens, which is primarily smoking or chewing tobacco, along with the human papillomavirus—the latter being specific really only to the oropharynx site. The vast majority of cases of head and neck cancer are caused by carcinogens such as smoking.

Within the subset of patients with oropharynx cancer, a large majority today are now known to be caused by the human papillomavirus. Detection of the HPV status is principally performed in the local hospital laboratories using an immunohistochemistry stain called p16, which reflects a surrogate marker for HPV status, in that p16-positive oropharynx cancers are known to be HPV-induced, whereas p16-negative cancers are smoking- or carcinogen-induced.

And it's clear that prognosis is poor for patients with HPV-negative head and neck cancers compared to those with HPV-positive

oropharynx cancer. For example, in locally advanced HPV-negative head and neck cancer, current therapy cures 50% or less of patients, whereas with HPV-positive oropharynx cancer, current therapy cures 80% or more of patients.

And the current treatment for HPV-negative disease principally includes surgery followed by radiotherapy or chemoradiotherapy. Whereas in HPV-positive oropharynx cancer, the current treatment is principally chemoradiotherapy.

It's important to consider the factors that are relevant to the selection of patients for perioperative pembrolizumab. This includes the histology. That means squamous cell carcinoma, site—that being oral cavity, larynx, oropharynx, and hypopharynx. Also, patients are to have locally advanced head and neck cancer and resectable disease, as determined by an oncologic surgeon.

In HPV-negative locally advanced head and neck cancer, we're speaking of clinical stages III and IVA, and for oral cavity, larynx, and hypopharynx, the decision would be independent of p16 status. Whereas for oropharynx cancer, we're speaking specifically of p16-negative disease. For HPV-positive oropharynx cancer, the focus here is on stage III disease, which is defined by resectable T4 disease.

Also, appropriate candidates will have a tumor that has a PD-L1 combined positive score of 1 or greater. Patients should have adequate organ and functional performance status, and no known contraindications to immune checkpoint inhibitors, including immunosuppressive therapy, autoimmune diseases, and organ transplant.

And finally, the role of cisplatin is relevant to these patients who've had tumor resections. In 2004, the result of two phase 3 trials established the importance of the addition of cisplatin to post-op adjuvant radiotherapy, which reduced the risk of local or regional recurrence and increased overall survival but had no impact on the risk of distant recurrence. The benefit of cisplatin was limited to patients with high-risk pathology, as defined by a positive surgical margin and/or extranodal extension.

Well, my time is up. Thanks so much for listening.

Announcer:
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