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Managing Immune-Related Adverse Events in the Perioperative Setting

Announcer:

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Dr. Adkins:

This is CE on ReachMD, and I'm Dr. Douglas Adkins. Today, I will discuss strategies for managing immune-related adverse events associated with perioperative immune checkpoint inhibitors in patients with locally advanced head and neck squamous cell carcinoma.

This slide demonstrates for you the proportion of patients who develop immune-related adverse events to perioperative pembrolizumab on the KEYNOTE-689 trial. As you can see, the vast majority of immune-related adverse events were targeted towards the thyroid and led to hypothyroidism in 24.7% of patients and hyperthyroidism in a smaller fraction of 8.9% of patients. Skin toxicity and pneumonitis occurred in a substantially smaller proportion of patients but are important for us to discuss today.

With respect to monitoring for immune-related adverse events, my recommendation at baseline, perform physical examination, blood counts, liver function tests, a serum creatinine, and a free T4 and a TSH. And then with every administration of the immune checkpoint inhibitor, to conduct a clinical exam, repeat liver function tests and serum creatinine, along with periodic testing with a free T4, TSH, and the blood count. On an as-needed basis, it's important to consider O2 saturation and chest CT scan testing if there's clinical concerns for pneumonitis, cortisol and ACTH for clinical concerns of hypoadrenalism, amylase and lipase for concerns for pancreatitis, a urinalysis for concerns of nephritis, and a troponin and CPK for concerns for myocarditis.

I'd like to discuss mitigating immune-related adverse events across the scenarios of thyroid disorders, pneumonitis, and skin toxicities. It's important to recognize that many, if not most, immune-related adverse events that occur with perioperative pembrolizumab are manageable by the oncologist. But there are occasions where one should consider multidisciplinary referrals as needed, such as the endocrinologist, dermatologist, or the pulmonary physician.

In my experience and in the clinical trial KEYNOTE-689, subclinical hypothyroidism or asymptomatic overt hypothyroidism were the most common immune-related adverse events associated with pembrolizumab. These conditions can be managed with supplementation by levothyroxine, and continuation of the immunotherapy drug is appropriate.

In the case of thyrotoxicosis or hyperthyroidism, most of these cases are asymptomatic, and patients can continue on their immunotherapy. And over time, most cases of initial onset hyperthyroidism will evolve into hypothyroidism and will require supplemental levothyroxine replacement.

Rash and pruritus are very common with pembrolizumab. In most cases, this is mild, and patients can be managed symptomatically with creams that could include corticosteroids or antihistamines—either oral or by skin application. Generally, immune therapy may be continued in mild rash and pruritus conditions.

Special note to discuss pneumonitis, which is infrequent but an important, potentially serious side effect of perioperative immune checkpoint inhibitors. Any grading of pneumonitis, if that is apparent, it's important to hold the immunotherapy, to assess the etiology of the pneumonitis, treat it, and then later on, when the patient is better and recovered, consider the possibility of reimplementing the immunotherapy based on clinical judgment.

Patient education is a key element of informing patients about the possibility of immune-related adverse events with perioperative pembrolizumab. I always tell patients the red flag symptoms that should be immediately reported to the MD. These include shortness of breath, cough, dyspnea on exertion—which could be signs of pneumonitis—or diarrhea, which could be signs of colitis.

Also, I share with patients that thyroid disorders and rash are the most common immune-related adverse events but are manageable without discontinuation of pembrolizumab.

Well, my time is up. I hope you found this overview useful. Thank you for listening.

Announcer:

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