Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/how-can-we-best-manage-iraes-during-adjuvant-icis-for-melanoma-a-case-based-approach/15782/

Time needed to complete: 1h 05m

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

How Can We Best Manage irAEs During Adjuvant ICIs for Melanoma? A Case-Based Approach

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Mitchell:
Hi, I'm Dr. Tara Mitchell, an Associate Professor of medicine at Penn's Abramson Cancer Center, and I'll be speaking to you today about how best to manage immune-related adverse events during adjuvant immune checkpoint inhibition for melanoma.

We'll start with the case of a 68-year-old woman with stage III melanoma receiving adjuvant PD-1 blockade. She reports new fatigue at cycle 4 of treatment and is noted to have a very elevated TSH on her routine pretreatment labs. This patient is demonstrating a clinical presentation of hypothyroidism which can occur in up to 20% of patients receiving PD-1 therapy and is usually irreversible. When we note the clinical onset of hypothyroid, which is confirmed by laboratory assessment, we began levothyroxine replacement, consider endocrinology referral for additional comanagement and education, and we monitor the TSH for improvement, as well as monitoring the patient for clinical improvement by the time of the next visit and in between visits as well. The treatment with adjuvant PD-1 blockade can be continued without interruption in the presence of this endocrinopathy, given that it is quickly reversible in terms of symptoms once replacement is started, and that the side effect itself is irreversible in that stopping therapy would not likely restore thyroid hormone production. High-dose steroids are not indicated for the treatment of hypothyroid, given that it is irreversible in nature and steroids do not improve the chance of recovery of thyroid hormone production.

Here's a case of a 44-year-old man with stage IIC melanoma receiving adjuvant PD-1 blockade who notes sparse, mildly raised erythematous rash on his chest and forearms which are not itchy or painful. This is the most characteristic presentation of a rash associated with PD-1 blockade. No intervention is necessary for a rash by itself in the absence of any painful severe lesions and in the absence of any severe or bothersome itching. We advise the patient that the rash will likely persist throughout treatment, but that treatment can continue without interruption. If itching is present, however, with or without rash, as itching can be seen as a side effect by itself or in addition to rash, and if it's bothersome, we start with supportive care measures such as moisturizer and less frequent hot showers. We can escalate to an over-the-counter strength topical hydrocortisone cream for a particularly bothersome spot treatment of certain areas, and escalate to a prescription strength topical steroid if their itching is not relieved by the over-the-counter strength. We also consider the use of over-the-counter antihistamines which are usually non-drowsy antihistamines for more diffuse and bothersome areas, and can escalate to prescription strength if not relieved. And finally, we can consider a low-dose prednisone usually 10 to 20 mg is adequate for an unresponsive, diffuse and severe itching or rash, and in some cases with more severe and diffuse involvement, a medium dose prednisone taper of 0.5 to 1 mg/kg daily and taper is indicated along with dermatology referral.

The third case is of a 71-year-old woman with stage IIIB melanoma receiving adjuvant PD-1 blockade who notes a new onset of fatigue, nausea, fevers after cycle 3 of treatment. Urgent labs same day identify a very low cortisol level below the lower level of lab reporting. Adrenal insufficiency occurs in up to 2% of patients receiving PD-1 therapy alone and is usually irreversible. Most commonly, it presents with nonspecific systemic symptoms such as the ones seen in this case of severe and new-onset fatigue, which is somewhat like a light switch turning off for the patient, new unexplained nausea, and in a patient with no evidence of disease who was being treated in the

adjuvant setting. There really shouldn't be any nausea related to disease, and so unexplained nausea, vomiting, fevers, all can be presentations of adrenal insufficiency, which are extremely important to recognize early and intervene immediately to prevent the onset of adrenal crisis which can be life threatening. We begin hydrocortisone replacement immediately in these patients along with patient education, and consider endocrinology referral for additional testing, monitoring, and patient education. Symptoms should resolve completely within 24 to 48 hours confirming AI as the cause of mild fatigue, nausea, vomiting, and fevers. And treatment can be continued without interruption, similar to other endocrinopathies, because the side effect is unlikely to be reversible and high-dose steroids are not indicated. Delayed recognition, again, as I mentioned, in adrenal insufficiency, can result in life-threatening adrenal crisis, shock, and multiorgan system organ failure, which should be recognized in any patient with immune therapy presented to the ER with these symptoms.

Finally, the case of a 35-year-old man with stage IIID. Melanoma receiving adjuvant PD-1 blockade who receives - who reports wrist, ankle, and knee pain and stiffness after cycle 2, and can no longer run. On physical exam, he's noted to have mild swelling of his knees noted on exam. Arthralgias without arthritis occur in up to 15% of patients receiving PD-1 therapy, and are usually reversible with stopping therapy. Mild joint pain can generally be managed with observation and/or NSAIDs as needed. However, severe pain with swelling, arthritis of joints with decreased functional capacity and decreased range of motion usually require prednisone. Low-dose prednisone can be tried initially, as these arthralgias that are severe arthritis with swelling and stiffness often are responsive to 10 to 20 mg per day, but if not responsive to low dose after 1 to 2 days, we escalate to the prednisone dose of 0.5 to 1 mg/kg daily and taper, as well as considering rheumatology referral if not able to taper steroids. Some patients require methotrexate or TNF blockade for ongoing arthralgias long after discontinuing therapy. And for this side effect, we have a low threshold for permanently discontinuing adjuvant therapy. In the absence of active disease, it's reasonable to stop therapy given that this side effect could result in a significant setback and quality of life, well-being, and function as in this case when the patient was no longer able to do his normal exercise or running.

In summary, patients should be evaluated labs, a history, and focused physical exam before every treatment cycle of adjuvant PD-1 blockade. The method of communication with the care team must be clear to all patients at all times during treatment starting with the first dose. They should know how to reach their care team, including nights and after hours and weekend hours. Endocrinopathies are common and irreversible, but do not require treatment interruption or discontinuation. And we have a low threshold for permanently stopping adjuvant therapy in patients who have a decline in quality of life, function, independence due to immunotherapy toxicity, and certainly in patients in which there's an organ-threatening adverse event, including acute liver, kidney, GI toxicity, or pneumonitis, any of which could become severe or life threatening.

Thank you for your participation.

Announcer:
You have been listening to CME on ReachMD. This activity is jointly provided by Global Learning Collaborative (GLC) and TotalCME, Inc. and is part of our MinuteCE curriculum.

To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.