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Managing Immunotherapy-Related Adverse Events during Adjuvant Treatment for Resectable Melanoma

Announcer:
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Dr. Lacouture:
Hello. My name is Mario Lacouture, and I am the Chief of Dermatology at NYU Langone in Long Island. I will be presenting on immune-related adverse events resulting from checkpoint inhibitor therapy.

These adverse events can affect any organ in the body. Therefore, it is important that a multidisciplinary team is involved in the management of these events in order to maintain quality of life, ensure consistent dosing of anti-cancer therapies, and maximize clinical outcome.

The development of immune-related adverse events may occur at any time during the course of therapy. On the left, you can see that cutaneous and gastrointestinal irAEs are the first to appear within the first to second month, followed by those of solid organs. On the right, you can see data from the adjuvant study in stage IIb/IIc melanoma patients treated with pembrolizumab versus placebo. As you can see in this figure, about a quarter of patients developed severe adverse events which may have limited therapy. Most commonly, as you can see here, were those affecting the thyroid, GI, and skin, but also fatigue, asthenia, and arthralgias were common. Importantly, most of these adverse events were manageable and patients were able to continue on therapy.

This figure illustrates in the adjuvant setting for melanoma with ipilimumab, the impact on quality of life. On the red line, you can see that with every infusion, there was a decrease in quality of life, which was sustained at a lower level even 2 years after therapy was completed.

In addition, therapies may affect consistent dosing; therefore, managing toxicities early on during the course of therapy is key. In this figure, you can see that the need for interruption or discontinuation of checkpoint inhibitors was necessary in between 10 to 20% of patients receiving monotherapy and about 40 to 60% of patients receiving combination therapies.

The management of adverse events has been highlighted and published in various journals as a result of guidelines issued by main oncology societies such as the American Society of Clinical Oncology, ESMO, SITC, and the National Comprehensive Cancer Network. These comprehensive guidelines are extremely useful for the management of adverse events and give you practical tools to manage them for both mild to moderate events as well as severe toxicities. In general, referral to a specialist is important for grade 3 events, whereas grade 1 or 2 events can be managed by the medical oncologist.

In terms of treatment outcomes, it is important to recognize that the majority of adverse events that are referred to a specialist, as illustrated here, for dermatologic events, are going to be moderate to severe. And the outcome will be positive in up to half of patients. About 1/3 of patients will have a modest outcome in terms of their toxicity, but they will benefit from specialized therapy.

In patients treated with a checkpoint inhibitor for lung cancer that needed their checkpoint inhibitor interrupted, about 1/2 of these patients upon rechallenge, did not develop a new irAE, and about 1/4 of them develop either a new irAE or a recurrence of the same irAE. Therefore, it is important to maintain therapy even when patients have interrupted their treatment.

Also important is to consider that the use of corticosteroids, as illustrated here for hypophysitis, may affect clinical outcome, affecting the anti-tumor efficacy of checkpoint inhibitors. And if the dose of prednisone is higher than 10 mg, it can also negatively affect overall survival.

Interventions targeted towards specific pathways involved in immune activation, as illustrated here, with commercially available agents are ideal, as they would be devoid of the complications of corticosteroids and ensure consistent dosing of therapy.

Two cases illustrated here of dermatologic irAEs treated with targeted therapies. On the upper panel, you can see a patient with a pruritic eczematous rash treated with the IL-4 inhibitor, Dupixent, showing a marked response. And on the left, a patient with a psoriasis type eruption treated with a biologic therapy. And after only one dose, you can see the significant improvement.

The results of this study that have been published this year show that with targeted interventions towards symptoms, you can improve outcomes. And this study was a meta-analysis of immune-related adverse events and the correlation with clinical outcome. And it turns out, as you can see, that patients that develop irAEs, especially endocrine, dermatologic, and gastrointestinal, tend to have a better outcome in terms of the anti-tumor effect than those who do not. Therefore, it is imperative for us to manage these adverse events so that patients can stay on therapy and derive the maximum benefit from their checkpoint inhibitors.

So to conclude, immune-related adverse events are expected and manageable in the majority of cases, most patients are able to complete their course of therapy, and an interdisciplinary and interprofessional approach is key with the use of targeted interventions and for counseling and support.

Thank you.

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