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Nectin-4-Directed ADCs in Bladder Cancer

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum and is titled “Nectin-4-Directed ADCs in Bladder Cancer”.

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

Dr. Iyer:
Antibody-drug conjugates, or ADCs, have been around for over 20 years. However, the first ADC wasn't approved in bladder cancer until just a few years ago. With ADCs finally in the treatment algorithm, patients have experienced significantly improved overall survival. But while the novel mechanism of ADCs allows for cytotoxic agents to be delivered to the cancer cells and limits the overabundance of toxicities, there are still adverse events that we care providers need to know how to manage. So let's dive right in.

This is CME on ReachMD, and I'm Dr. Gopa Iyer.

Enfortumab vedotin, or EV, is an ADC that binds to nectin-4, a protein expressed on the surface of most bladder cancers, and delivers an MMAE [monomethyl auristatin E] cytotoxic payload. Common adverse events related to EV include peripheral neuropathy, skin rash, ocular disorders, and hyperglycemia. Most patients receiving EV experience peripheral neuropathy related to the MMAE payload. Sensory neuropathy is more common than motor neuropathy and frequently presents as numbness in the fingers and toes.

Strategies for managing neuropathy include dose interruptions and/or dose reductions, as well as discontinuation of therapy in order to prevent permanent side effects. And the specific intervention should be based on CTCAE [Common Terminology Criteria for Adverse Events] grading criteria. Early recognition of peripheral neuropathy is critical to prevent worsening of side effects, and patients should be advised to report any symptoms promptly.

The most common skin-related symptoms associated with EV are maculopapular rash, pruritus, changes in skin pigmentation, and dry skin. While most skin changes are mild and resolve with topical therapies, up to 13% of patients have experienced grade 3 skin reactions, and severe and fatal cutaneous adverse reactions such as Stevens-Johnson Syndrome have been reported.

A multidisciplinary approach is essential to successful management of rash, including referral to a dermatologist whenever possible. Patients should report any cutaneous symptoms promptly. Use of sunscreen and moisturizers can be quite effective for mild symptoms such as pruritus and dry skin, while topical steroid creams are useful in managing rash.

Ocular toxicities that have been reported with EV most commonly include dry eyes and blurry vision. While a baseline eye exam is not required with EV, patients who have known ocular conditions may benefit from ophthalmologic monitoring while on treatment.

Hyperglycemia is another side effect observed in approximately 11% of patients on clinical trials of EV, with some patients experiencing diabetic ketoacidosis and even death. The incidence was higher in patients with preexisting hyperglycemia, such as from diabetes, and in patients with a higher body mass index and an elevated hemoglobin A1c. Patients with a baseline hemoglobin A1c greater than or equal to 8% were excluded from the clinical trials of EV. Blood glucose levels should be monitored while on EV, and EV should be held

for blood glucose levels greater than or equal to 250 mg/dL.

Unfortunately, that's all the time we have today. So I want to leave you with this final take-home message. Both EV and SG [sacituzumab govitecan] have specific side effect profiles that are related in part to the different cytotoxic payloads of these compounds. It is essential for care providers to familiarize themselves with these toxicities and monitor for them routinely in patients who receive these drugs. Most of the side effects of EV can be managed successfully if caught early and treated immediately. And a multidisciplinary approach is highly recommended for the management of these toxicities.

Thank you for your attention and have a wonderful day.

Announcer:
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