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How Do You Manage Enfortumab Vedotin (EV) Related Adverse Effects?

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

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Dr. Gupta:
Hello, my name is Dr. Shilpa Gupta and I'm a medical oncologist specializing in genitourinary cancers at the Cleveland Clinic Taussig Cancer Institute in Cleveland, Ohio. Today, I'll talk about how to manage and enfortumab vedotin, or EV, related adverse effects.

We'll start with a case discussion. A 65-year-old woman received gemcitabine and cisplatin for metastatic urothelial cancer. Had a partial response after six cycles but developed grade 1 peripheral neuropathy. She then received avelumab and progressed after three cycles and was started on enfortumab vedotin at 1.25 mgs per kilogram dose on day 1, 8, and 15 every 28 days. Unfortunately, she developed worsening of peripheral neuropathy which was now a grade 2 after three cycles.

What will you do next? The options are to continue EV at the same dose, B to continue EV at reduced dose of one mg per kilogram, and C to withhold EV until neuropathy improves to grade 1 and then resume it at a lower dose of one mg per kilogram. The right option here is answer C because peripheral neuropathy can be disabling and early dose interruptions and dose reductions can help prevent development of grade 3 or higher neuropathy thus allowing patients to remain on the treatment regimen longer, especially when it is causing clinical benefit.

Management of peripheral neuropathy is very important, and we need to monitor patients throughout their course while they're receiving EV. In my practice, if patients develop grade 2 peripheral neuropathy, I withhold EV until it improves to grade 1 and then resume at a lower dose. And again, one can use investigator's discretion while the package insert mentions resuming the dose at the same level. I tend to reduce it at a lower dose because peripheral neuropathy can become quite disabling and we need to permanently discontinue EV for grade 3 or higher neuropathy.

Our second case is of a 70-year-old man who is on EV at 1.25 mgs per kilogram dose, develops a generalized maculopapular rash over trunk, back, and extremities. The rash is itchy. What will you do next? Continue EV at current dose or continue EV at reduced dose or option C, with hold EV, prescribe topical steroids and antihistamines, refer to dermatology and do not resume EV until rash resolves to grade 1 or less. The right answer here is option C and, in general, the rashes can be very serious and life-threatening. We need to monitor patients for signs of skin reactions and mucosal abnormalities throughout their course on EV. Topical steroids and antihistamines should be used for mild reactions and for severe reactions, consult dermatology and consider skin biopsy. Withhold EV for grade 3 or higher reactions and discontinue it permanently for grade 4 Stevens-Johnson or toxic epidermal necrolysis or recurrent grade 3 skin reactions.

Our last case is of a 73-year-old man on EV, 1.25 mgs per kilogram dose. Has a BMI of 35 and blood glucose level of 320 mgs per deciliter on the day of EV treatment. Notably, the patient is not a known diabetic. What will you do next? A, continue it at the current dose and monitor blood sugars. Continue EV at reduced dose and monitor blood sugars or withhold EV, check HbA1C, refer to

endocrinology for blood sugar management, and then resume EV once blood sugar's well controlled. The right option is the option C. There is a risk of development of diabetes mellitus and diabetic ketoacidosis with EV, and we should withhold it for blood sugars greater than 250 mgs per deciliter on any treatment day.

With this blood sugar control, the patient resumes EV. He returns to clinic for the next cycle endorsing blurred vision and increased tearing and discomfort. What will you do next? Option A, continue EV at current dose and recommend artificial tears. Option B, continue at reduced dose and recommend artificial tears. And option C is to withhold EV, refer to ophthalmology, and option C is the right option cause there can be ocular disorders associated with EV, reported in about 40% patients who were receiving EV and these are usually like keratitis, blurred vision, keratopathy, conjunctivitis, et cetera. Time to onset is within the first two months. We should monitor for any signs or symptoms throughout treatment. Consider prophylactic artificial tears. However, if symptoms have developed, ophthalmology consultation is a must. If these symptoms don't get better, consider steroids topically if indicated and consider holding and/or reducing the dose for symptomatic ocular disorders. Thank you.

Announcer:
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