Transcript Details

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Incorporation of guideline-concordant care for first-line treatment of a patient with metastatic urothelial carcinoma

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

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Dr. Duran:
Hello, this is CME on ReachMD and I'm Ignacio Duran.

Dr. Srinivas:
And I'm Sandy Srinivas.

Dr. Duran:
We're going to start by presenting a clinical vignette to try to understand treatment in first-line metastatic urothelial cancer with a combination of enfortumab vedotin and pembrolizumab.

This case is a 67-year-old gentleman. He has a past history of smoking. He has high blood pressure, well controlled with medication, and no other comorbidities. ECOG performance status is 1 when he presented to the clinic, and he was diagnosed because of left flank pain and hematuria with an upper tract urothelial carcinoma in his left kidney with extensive lymph node dissemination. This was considered to be T4, N3, M0, so a stage 4 upper tract urothelial cancer.

The patient was assessed in the clinic and it was considered that he was eligible to receive enfortumab vedotin and pembrolizumab, and we can discuss later on what is the evidence behind. He started treatment. Initially, it was well-tolerated, but since cycle 2, the patient started to refer fatigue that was graded as a Grade 1, and he presented some skin toxicities, mostly alopecia, that reach a Grade 2, some hyperpigmentation, some dry skin and pruritus. Those were considered as a Grade 1.

The good news is, in the first CT scan, there was already a significant reduction of the target lesions that would qualify as a partial response. So, the patient continued treatment and he continued to evolve in a positive way. It's true that he required dose-reduction later on due to some peripheral sensory neuropathy. He continued to present a skin tox that we were able to manage with topical treatments and sometimes short courses of systemic steroids, but nothing really serious. Never any signs of really severe skin tox.

The patient handled well these side effects after the dose-reduction, and right now he has received more than 12 cycles, and he continued treatment with a partial response. So, this is an example to introduce our discussion. So, back to you, Dr. Srinivas.

Dr. Srinivas:
That's a great case, Dr. Duran. It's quite common. This is a very typical presentation for what we see in our clinics, too. And it's a great example for why enfortumab vedotin with pembrolizumab has really got a category 1 recommendation from the NCCN for patients with frontline metastatic urothelial cancer. And it is based on EV-302, as your patient has also seen the benefit, the overall response rate for this regimen was around 68%, and the PFS was more than a year, around 12.5, and a doubling of overall survival at around 31.5 months

compared to chemotherapy. An interesting part was this benefit was seen irrespective of whether patients were cisplatin eligible or not.

Now, for your patient, EV-302 was for patient with bladder primary, but I think a third of patients were included in EV-302 that were upper tract. So, it's interesting. Peripheral neuropathy is definitely a common side effect that we see in our patients. What has your strategies been in terms of mitigating this side effect?

Dr. Duran:
Well, thank you for the comment. And as you said, yeah, 30% of the patients in EV-302 were upper tract tumors. So, perfectly reasonable election or choice for these patient, EV + pembro. And as you mentioned, peripheral sensory neuropathy is going to be there in about half of the patients. So, I think there area key point here, and the key points are education. I think we need to educate our patients from the get-go. We need to let them know what they could expect in terms of toxicities. We need to educate family members as well, and we need to educate caregivers, doctors, nurses, etcetera. I think if you give a proper information, it's easier to handle this. If you inform your patients that they may need a dose reduction along the duration of treatment, I think they're better prepared.

What I do in my clinic in a practical basis is I test how they are from a sensory perspective. I throw them, or I actually give them a pen to see if they can grab it. I put a piece of paper on the table to see if they can grab it, or I ask them if they can button and unbutton their shirt. That's the practical way of seeing whether this is a Grade 1 one or a Grade 2 toxicity. As soon as I see the peripheral sensory neuropathy getting worse and being limiting for daily activities, then we stop, and we dose reduce. But with a well-informed patient, it's not a problem. If you don't inform your patient, then it comes frustration and concern about lack of activity.

Dr. Srinivas:
Yeah, I couldn't agree with you more about the educational aspects because many of our patients, when they see this kind of a response, they are afraid that we may stop therapy. So, I think really, educating them that dose reduction and dose hold is part of what was done in the trial and that would be very applicable to them.

I think to summarize, with the great response that we see with EV-302, we want our audience to be informed about the side effects to watch out for, which sounds like it would be mostly skin rash, some fatigue, definitely neuropathy, and how we pay close attention to dose reduction and dose holds.

Dr. Duran:
OK, perfect, Dr. Srinivas. I think that's a great summary. So, the message is, enfortumab vedotin is a quite useful regime with quite impressive data that is actually going to change the way we treat patients, but we need to inform them and inform our caregivers about potential toxicities to improve the management of this combo.

Thank you everyone for your attention.

Dr. Srinivas:
Thank you.

Announcer:
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