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Emerging targeted therapy combination strategies in genitourinary malignancies

Announcer:
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Dr. Duran:
Well, this is CME on ReachMD, and I'm Dr. Ignacio Duran. Today I will provide a brief overview of emerging practice changing directions in genitourinary malignancies involving targeted therapies and combinations.

I've chosen to talk about urothelial cancer. There have been many changes and the arrival, the incorporation, of many treatment options for such a difficult population of patients, such as the advanced urothelial cancer patient community. I think deserves this particular attention. So, in the next 5 minutes I'm going to try to put all the attention in one challenging population that we have in our clinics, which is the group of patients that cannot receive cisplatin-based chemotherapy. What we call cisplatin ineligible patients. And in order to do so, I'm going to start by reviewing the data of the study named EV 103.

So, EV-103 is a large and complex study that actually has many different cohorts but was designed to test EV or EV in combination with pembrolizumab in different settings for patients who were considered cisplatin ineligible. This study includes the phase 1 component where the dose for further cohorts was defined and we call that the dose expansion cohort. And then, there are multiple different cohorts, including from cohort A to cohort L, but today I'm going to talk about dose expansion cohort, cohort A, and cohort K.

The dose expansion cohort included different group of patients, but actually it was the part of the study that we needed to define the recommended phase 2 dose of EV + pembro. And already in that dose expansion cohort, we saw remarkable activity of EV + pembro. In cohort A, we tested EV + pembro in a single-arm study with about 40 patients in first-line cis ineligible. And in Cohort K, what we did is a small, randomized phase 2 study comparing EV + pembro versus EV. Let me get into a little bit more detail. The dose expansion cohort, cohort A, altogether included 45 patients. And in this cohort, what we saw, it was a very powerful signal that I think has been the foundation for further studies. And we already saw 73% of overall response rate with about 15% of complete responses. And we're talking about a population of patients that is normally quite challenging in the clinic because of the lack of good options.

If we move to the other cohort, cohort K, again, we saw remarkable activity, and in this cohort, the confirmed overall response rate was about 64.5%, and 45.2% respectively in the doublet, EV + pembro versus EV monotherapy. So, actually it was one of the first signs that EV + pembro was actually quite an active combination. And in fact, this data led to approval and gave access to North American physicians to this combo to start using it in such a population. On top of the activity, it needs to be commented that there are some adverse events that come with these combination, and in cohort K, what they saw as the most common Grade 3 or higher treatment-related adverse events was basically skin tox with maculopapular rash in about 17% of the patients, fatigue, and very small numbers of neutropenia. And actually, we're started to know some data about peripheral neuropathy that in fact has turned as one of the limiting factors in clinical practice. So, as I said, this data was critical and actually led to be able to use EV + pembro in that difficult population of patients.

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And I think this exciting data of the remarkable activity of antibody drug conjugates like EV + pembro in the context of urothelial cancer has led to look into further combinations, and we need to keep in mind that there are other studies ongoing right now that are testing EV + pembro, or other combos in different settings. And we need to take into account that there are multiple studies testing EV and other antibody drug conjugates in the perioperative setting. And also, I'd like to bring your attention one step further I should say, which is, combining not only one antibody drug conjugate with pembro, but two antibody drug conjugates. And this is what we call the DAD trial, which is the double antibody drug conjugate trial. And that was conducted at the Dana-Farber combining enfortumab vedotin + sacituzumab govitecan, and that revealed some encouraging results in terms of efficacy and overall response. Now, they're moving to one step further, which is DAD I/O which is adding to the doublet of ADC's and I/O component with pembrolizumab.

So, in summary, to conclude my 5 minutes around cisplatin ineligible patients and doublets, I think we have actually defined through some consistent data across different studies that EV + pembro is a very valid option to treat this difficult population. And we're not stopping here, we're doing other studies not only in the metastatic setting, but in the periop setting, and also combining further drugs and trying to test the value of triplets in this context.

Thank you very much.

Announcer:
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