Transcript Details

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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Clinical evidence driving guideline recommendations for monotherapy in the second-line or later setting in metastatic urothelial cancer

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

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Dr. Srinivas:
This is CME on ReachMD and I'm Sandy Srinivas.

Dr. Duran:
And I'm Dr. Ignacio Duran.

Dr. Srinivas:
Dr. Duran, can you take us through the data that support guideline recommendations for monotherapy in the second-line or later-line setting in metastatic urothelial cancer?

Dr. Duran:
Absolutely. Thank you. This is a great point, and I think it's a situation that we're going to confront more and more often in our clinics. So, let me share with you briefly what is the evidence. And in order to do so, I'm going to divide the information in four blocks. We're going to talk briefly about patients post chemotherapy, probably a population of patients that is going to get smaller and smaller. I think the highest level of evidence for the treatment after progression to cisplatin-based chemotherapy is actually checkpoint inhibitor with pembrolizumab, and this is based on KEYNOTE-045 that was already communicated in 2017. Some other studies, other phase 2, or even some pooled analysis from phase 1 also demonstrate activity for other checkpoint inhibitors. But I think as I said, after chemotherapy, pembrolizumab is the drug with the highest level of evidence. But what if my patient only received checkpoint inhibitor as single agent in the first line? Then, we have to go to EV-201. It's a study that's tested enfortumab vedotin in different populations. And in cohort 2 of EV-201, EV was given to patients that were cisplatin ineligible and who have progressed after checkpoint inhibitor only. This data has been already published by Yu and colleagues in 2021, and EV demonstrated remarkable responses of around 52% actually, in this context.

Next, let me focus very briefly on the data around patients who have progressed after chemotherapy based on platinum, and then immunotherapy either maintenance or as second-line. Here, we're got to talk about a bigger study, EV-301. There, we tested within a phase 3 context, the hypothesis of whether EV, even in days 1, 8, and 15 at 1.5 or 1.25 milligram per kilo would be superior to chemotherapy. And in this context, the answer was clearly positive, and there was a 30% reduction in the risk of death and a median overall survival close to 13 months for the experimental arm of enfortumab vedotin.

These outcomes have been later confirmed with longer follow-up, and I think it's very useful and a very interesting piece of information to inform how to treat our patients in the clinic.

Lastly, in my last 15 seconds, mention a population of patients that I think is also relevant. And are those patients who have FGFR alterations, either mutations or fusions. We need to keep in mind the data from studies like BLC 2001 already published in 2019, that tested erdafitinib with positive outcomes. Although, in the randomized fashion in THOR cohort 2, erdafitinib was not able to be superior to pembrolizumab, so that's information to keep in mind as well.

Thank you.

What do you think about how this data that I briefly summarized can inform the current guidelines?

Dr. Srinivas:
Of course. Thank you. I mean, I think what you're saying is that the most active agents we have in urothelial cancer are basically immunotherapy. We have enfortumab vedotin and erdafitinib for those who have an FGFR mutation. So, I think the NCCN guidelines takes that into consideration for second-line. Really, looking at patients, what prior therapy they have had, we take into consideration performance status, medical comorbidities, the platinum eligibility and time since their last therapy.

So, as you said, I think in patients who have had prior chemotherapy, and who have not had immunotherapy, checkpoint inhibitors definitely have their place as in the second-line setting. But I think as we see more EV + pembro become frontline, it becomes a challenge about what the second-line would be. And I think there, the guidelines take into consideration doing testing, and if patients are positive for susceptible *FGFR3* genetic alterations, to consider erdafitinib.

For those patients who have had prior immunotherapy and who have never seen enfortumab vedotin, again, per your discussion, I think EV has a place for second-line in patients who have not been previously exposed.

Dr. Duran:
Yeah, I think this is a very interesting field right now, and I think the key point, as we very well summarized and I think it's very well expressed in NCCN guidelines, is taking into account what has been the treatment received in the first-line, and the whole clinical context of the patient that is going to let us select the subsequent therapy, and also, take into consideration the genomic alterations. I think that's the way I see it and I think that's the way NCCN guidelines actually summarize this.

Dr. Srinivas:
Well, that's all the time we have today. Thank you for a great discussion, Dr. Duran, and thanks to our audience for listening.

Announcer:
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