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Selecting the Optimal ICI Partner for First-Line Treatment of Unresectable HCC: CTLA-4 vs VEGF Inhibitors

Announcer:
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Dr. Abou-Alfa:

This is CME on ReachMD and I'm Dr. Ghassan Abou-Alfa from Sloan Kettering Cancer Center in New York.

Dr. He:
This is Dr. Ruth He from Georgetown University Hospital from Washington, DC.

Dr. Abou-Alfa:
We now have two FDA-approved combination regimen involving immune checkpoint inhibitors, also known as ICIs for first-line treatment of unresectable HCC.

Ruth, how would you select the optimal ICI partner between CTLA-4 and VEGF inhibitors?

Dr. He:
Here are some clinical factors I would consider during the treatment selection. And the number one priority is try to really judge what the portal pressure is. So, if patient has severe cirrhosis, increased portal pressure presenting as enlarged varices, and/or if patient has portal vein thrombosis, which also can result in increased portal pressure, and those patients are at the risk of bleeding. And of course, those patient needs to have an endoscopy to evaluate the varices and to see the need of treatment for those varices.

I probably would stay away from anti-VEGF therapy, with concerns about the bleeding risk.

Ghassan, what other factors would you consider selecting the optimal immunotherapy partners?

Dr. Abou-Alfa:
Well, thanks Ruth. I totally agree with you. No doubt that if there are varices, definitely we need to avoid anti-VEGF. People can die. And it's very important for our colleagues to make sure that they scope the patients before using any of the anti-VEGF therapies like the bevacizumab. On the other hand, there could be other components which are really critical over here. We have to remember that there is a certain incredible potency for the anti-CTLA-4 that you should not ignore. After all, one dose only as we saw in the durvalumab plus tremelimumab, or what we're calling the STRIDE regimen, can really impose a high tumor burden, because interestingly, even the anti-CTLA-4 being tremelimumab is way more potent than even CD28, which is the one that enhances activity, or the anti-PD-1 and PDL-1.

No doubt, that performance status is going to come play, exactly as you said. Remember, the patients with potential for varices are the patients with potential portal vein thrombosis, potential with impact in regard to liver function, which interestingly, and for example, the combination with the anti-CTLA-4, we didn't really care much about that because patients will just be eligible for the therapy anyway.

And of course, there is a patient preference. We have seen, of course, patients go one way or the other. But interestingly, less visits to the clinic always is favored, like for example, in this STRIDE regimen with only one visit per month.

Dr. He:
In clinic, I also realize a lot of patients actually have proteinuria as a result of hypertension or diabetes. And anti-VEGF therapy may increase the risk of having worsening proteinuria. So, that's something I always will check. If patients already have significant amount of proteinuria and usually, if it's 1000 milligrams per 24-hour urine collection, I probably would also be very cautious when I start anti-VEGF therapy.

Dr. Abou-Alfa:
Well, for our colleagues, as you can see, definitely we can look at things from different perspectives. But you noticed both of us are kind of like rather cautious when it comes to the potential adverse events or, number two, in regard to the applicability of the therapy. In regard to the applicability of the therapy, Dr. He just provided us with a very robust analysis of the concern about the varices, and please, please again, I reinforce that one more time, make sure you scope the patient when you start to do anti-VEGF therapy. People can bleed.

Number two, in regard to the adverse events, know that less adverse events, less potential inconveniences. As we heard from Dr. He in regards, for example, the opportunity which can happen with anti-VEGF. Of course, the patient will be kind of happier and able to do the therapy, especially if it's not that frequent, like for example, with the monthly basis only with the durvalumab/tremelimumab or STRIDE regimen.

Well, that's all the time we have today. Thank you for a robust discussion, Dr. He, and thanks for the audience for listening.

Announcer:
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