Transcript Details

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Guideline-recommended first-line treatment with immunotherapy and targeted therapy combinations in renal cell carcinoma

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. Xu:
And I'm Vincent Xu.

Dr. Srinivas:
Dr. Xu, can you take us through the data that support guideline recommendations for first-line treatment selection in advanced clear cell renal cell carcinoma? But maybe we can focus on the immunotherapy and targeted therapy combinations?

Dr. Xu:
Absolutely. I think we're in such a great time right now for clear cell renal cell carcinoma because we have options for our patients. In the last few years we've had four excellent frontline options, all of which have shown PFS and OS benefit over sunitinib, which was the old standard of care. These four combinations include three VEGF TKI plus PD-1/L1 combinations including cabozantinib and nivolumab from CheckMate 9ER, lenvatinib plus pembrolizumab from CLEAR, axitinib plus pembrolizumab from KEYNOTE-426, and ipilimumab plus nivolumab which is the only IO/IO combination with a PD-1 and CTLA4 antibody, which was CheckMate 214.

All four of these combinations are excellent choices in the first line for patients. And more and more, we're seeing that this decision can be made in all categories of IMDC risk. We used to think that ipi/nivo was only for intermediate and poor risk, but now with the updated NCCN Guidelines, it's also recommended in favorable risk.

When we're looking at these trial options for our patients, we're really looking at the pros and cons between these regimens. And the first decision point is, does this patient need IO/TKI versus IO/IO. And when we compare these, the three IO/TKI regimens are similar in that they have high overall response rate, but they require ongoing VEGF receptor TKI, which can be difficult for patients in the long term. By contrast, when we look at ipilimumab plus nivolumab, there is a lower overall response rate, but there are a subset of patients with durable responses and even treatment-free survival after 2 years. So in general, I pick IO/TKI for my patients who are highly symptomatic, really need that immediate response to improve their quality of life. Whereas I pick IO/IO among patients who can afford to have a little bit higher risk of disease progression but may want to have that chance of a durable response.

Now, when I think between the different IO/TKI regimens, I really look at the differences between TKIs. For example, lenvatinib has a little bit more FGFR activity and a great upfront response rate when combined with pembrolizumab. On the other hand, cabozantinib has a little bit more AXL and MET activity and has a great response rate in bone and brain metastases when combined with nivolumab.

Axitinib is different from the others in its very short 6-hour half-life, and so I really use axi/pembro when I feel like I might need to stop the TKI at a very short notice.

Dr. Srinivas:
Well, great points that you bring up. I want to take what you have said and sort of see how it incorporates into our NCCN Guidelines. And I think to your point, NCCN divides these patients into favorable risk and intermediate and poor risk. And all of these options get category 1 for the intermediate and poor risk because there's high-level evidence and these trials included a lot of these patients.

More recently, NCCN included ipi/nivo also for favorable risk. So I think, for our viewers today, for a patient who comes in with a metastatic clear cell RCC like you illustrated, we have some incredible number of options. My take is that I think you need to pick the TKI that you're most comfortable with, where we know that we have the ability to manage the adverse events, keep people on appropriate dose so that they can have a good response, and yet enjoy your quality of life, because this is treatments that have been associated with improvement in longevity, where patients are going to be staying on this therapy for a while. To your point, I do think the dual IO therapy does afford a treatment-free interval, which I think many of our patients welcome as well.

Dr. Xu:
Thank you, Dr. Srinivas. It's so great to be in a situation where we have multiple options for our patients. It gives us a lot to talk about, but it's good to give patients these options.

Dr. Srinivas:
This has been brief, but a great discussion. I hope we gave you something to think about, and thanks so much for tuning in.

Announcer:
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