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Applying Current Guidelines in the First-Line Treatment of MSI-H/dMMR mCRC—A Case Discussion

Announcer:
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Dr. Parikh:
Hello. I'm Dr. Aparna Parikh. And now, we're going to be talking around how we select first-line therapy for MSI-high colorectal cancer patients based on the current guidelines. Let's explore this in a case vignette.

This is CME on ReachMD.

So I recently had a patient in my clinic. I see a lot of patients, unfortunately, that have young-onset colorectal cancer. And many of these MSI-high patients, especially who are younger, often have what's called Lynch syndrome.

And so it's not entirely surprising that you see these patients a little bit younger. So this was a young woman in her 40s and she presented with several months of kind of rectal bleeding, abdominal discomfort. Notably, she did have a family history of GI cancers with her mother and grandmother both having colorectal cancer. But unfortunately, unbeknownst to them, there was actually what was found to be a germline alteration in MSH6.

So workup led her to find a colon mass, a right-sided tumor, and the time I met her, her bowel movement caliber was getting smaller and smaller. She was having a hard time kind of passing stool; her abdomen was getting a bit more distended. And on imaging, not only did she have that right-sided tumor, she was found to also have liver metastasis as well as a few lung nodules.

So this is a patient that has kind of multifocal colorectal cancer with disease now in a couple of different organs, the liver, the primary tumor, lungs that were suspicious. And now we are sort of faced with what treatment options to give her. So first and foremost, I think, with colorectal cancer, you always want to think around is there a path towards a cure for these patients? And we can be quite aggressive about curative approaches for patients who have resectable disease. But nonetheless, especially with patients, even if there's a path towards rendering this young woman over time NED, first and foremost she warrants systemic therapy.

So how do you think about systemic therapy for these patients? There are several options for first-line patients with immunotherapy in the metastatic MSI-high setting, and those options include monotherapy with PD-1 inhibitors or combination therapy with CTLA-4 and PD-1 as well. And so both are reasonable options, again, based on the data that we've seen to date from the KEYNOTE-177 data. We also have data from CheckMate 142 and then data from CheckMate 8HW. Looking again at the CheckMate studies to date have shown the combination data versus chemo in 8HW, and CheckMate 142 just showing combination data. So both are reasonable approaches to thinking about this patient.

For this particular patient, I ended up deciding to use doublet immunotherapy. And the reason being is that she did have a good amount of disease burden in her liver. And I think more importantly is that I wanted to try to get a quick response because I was worried that she was potentially in danger of obstructing soon. And to try to avoid a kind of emergent or even kind of semi-urgent diversion, if you can get

a fast response rate and an improved response rate, although, again, we don't have yet PFS or survival data comparing the two options with monotherapy and doublet therapy yet, we do know that doublet therapy does give you a higher overall response rate. And so given that the response rate is a little bit higher, opted to do the combination therapy for this patient. But again, a monotherapy would be very reasonable and both appropriate per the guidelines.

This patient ended up having a tremendous response and is now in a position, actually, given the degree of her response, where we are actually thinking about surgical approaches for her. So gives you, hopefully, a sense of how to think about the different first-line options for these patients because there are, but noting that there is a nonresponse rate to immunotherapy, there are patients that just don't respond, but still standard of care would be to absolutely still try immunotherapy first and reserve chemotherapy for patients who do not happen to respond. But again, the majority of patients will derive some benefit.

Thank you for joining me for this case discussion. I hope this will help you utilize the current NCCN Guidelines when choosing the appropriate therapies for your patients.

Announcer:
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