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Case Consult: Current Standards and Emerging Directions in BRAF-Mutant mCRC Care

Announcer:
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Dr. Kopetz:
This is CME on ReachMD, and I'm Dr. Scott Kopetz. Here with me today is Dr. Cathy Eng, a colleague and friend, and delighted that in this episode we'll be discussing a patient case example in the first-line BRAF-mutated metastatic colorectal cancer.

Dr. Eng, what can you tell us about this patient?

Dr. Eng:
So actually, this is something that I have seen in my clinic. You have a young patient in your clinic with a profound tumor burden, notably of the liver and other areas of involvement, and you note that they basically have a right-sided tumor that may still be intact. And this is what this gentleman was that I have in my clinic. He'd had significant weight loss, just did not feel very well at all. And we ordered NGS immediately, both blood and tissue, and because we were concerned about the possibilities—we knew he was MSI stable, that had been already conducted when the pathology had been reviewed at our institution and as per outside report it was confirmed. And we noted that when the NGS blood came back, he had a BRAF V600E mutation. And as you know, this is less than 9% of our patient population. And this patient was appropriate for therapy.

And we happened to have the BREAKWATER study available to us at that time, which was for newly diagnosed BRAF V600E-mutant tumor types, metastatic colorectal carcinoma. And we enrolled him to the trial. Really, the patient is doing well. And the patient received FOLFOX plus encorafenib plus cetuximab in the frontline setting.

And a dramatic change already in his clinical symptoms. He had a reduction in just constitutional symptoms, had increased appetite, increased energy level, and decreased tumor pain. So really, just incredible benefit.

Dr. Kopetz:
Well, that's great to hear. And how was the patient's tolerance of the therapy?

Dr. Eng:
So the tolerance, I would have to say, was extremely good. The rash was not as severe as normally we would expect for cetuximab alone or cetuximab in combination with irinotecan. And otherwise, adjusting a little bit for some diarrhea, really no major issues. Overall, the quality of life was improved with the regimen.

Dr. Kopetz:
That's wonderful. And I think that really kind of mirrors what we see in the overall population with the substantial improvement in overall survival. I think it's heartening that we are seeing that this is now FDA-approved. This is part of an FDA Project FrontRunner, which is a new initiative to approve first-line therapies on the basis of response rates that then get them confirmed with PFS and OS, as we heard at ASCO this year. So we're delighted this is now an option for first-line patients.

Cathy, what's your anticipation about how ESMO and the European regulatory authorities will approach this data?

Dr. Eng:
Yeah. I mean, the data from BREAKWATER is pivotal, as mentioned, in regards to the overall survival of 30.3 months relative to standard of care chemotherapy, which historically has always been between 12 and 15 months. And that was confirmed in this trial. And I would hope that the ESMO guidelines will be revised shortly.

Currently, the guidelines that we have are a little outdated, obviously, but I'm sure they will be revised. But currently it states, if you have a BRAF patient, you should receive FOLFOXIRI plus bevacizumab or just doublet chemotherapy plus bevacizumab, and then in the second-line setting or in the refractory setting, they include encorafenib and cetuximab.

But here, I think things are going to be completely revised, and the frontline setting will be FOLFOX or oxaliplatin-based therapy with encorafenib and cetuximab based upon these results alone. So I think it's going to be a dramatic change for ESMO guidelines, and then obviously this will impact also the Asian guidelines as well.

Dr. Kopetz:
Well, that's great. And I think, important to acknowledge that making progress in the BRAF V600E patient population. Of course, the big questions that I know you and I both get is, what do I do with these other BRAF mutations? And I think here we just know that we've got to come up with some new treatments beyond encorafenib and cetuximab to really try to target those. But an area of active research.

So thank you, Cathy, for sharing this wonderful patient case, and thank you all for listening. We'll see you next episode.

Announcer:
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