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From Guidelines to Practice: First-Line Treatment Choices in mCRC

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Dr. Seligmann:

Hello, this is CME on ReachMD. I'm Dr. Jenny Seligmann. It is my pleasure to be joined by Dr. Fortunato Ciardiello.

We're going to get straight into it. We're going to talk about first-line treatment choices in metastatic colorectal cancer and particularly for those who are RAS and BRAF wild-type. So would you mind giving your views on what is the optimal management for these patients, please?

Dr. Ciardiello:

Thank you, Jenny. About 40% of patients with metastatic colorectal cancer have a disease that is both RAS wild-type and BRAF V600E wild-type. For these patients now, there is a cumulative series of evidence from different pivotal phase 3 clinical trials that show that a chemotherapy doublet, either FOLFIRI or FOLFOX, plus cetuximab or panitumumab, the 2 anti-EGFR monoclonal antibodies, are the preferred therapeutic options for first line, especially for patients whose primary tumor is located in the left side of the colon or in the rectum.

So for these patients, all international guidelines, in particular the ESMO clinical practice guidelines, are clearly stating this. And I would say that these come from original trials, like the pivotal CRYSTAL trial, now with more than 10 to 15 years of data that have been presented, in which additional cetuximab to FOLFIRI clearly showed a better response rate, a better median progression-free survival, better overall survival in these subgroup of patients.

Similarly, we had the same data with FOLFOX plus panitumumab in the PRIME trial. Whereas, we have also trials to add comparison between either cetuximab and panitumumab on one side and bevacizumab, the anti-VEGF monoclonal antibody on the other side, were made. And in all these trials, chemotherapy doublet, either FOLFIRI or FOLFOX, plus the anti-EGFR monoclonal antibody, were superior to bevacizumab combinations, at least for RAS/BRAF wild-type patients, with primary tumor easily located in the left side.

Dr. Seligmann:

So we talk about the two aspects of this journey in personalized medicine. So number one, our predictive biomarkers have got better, but there is the interesting conundrum on primary tumor location.

So what is your management of a right-sided patient with RAS and BRAF wild-type? What's your recommendations, usually?

Dr. Ciardiello:

The difference between anatomical site is a surrogate of molecular biomarkers that will be either altered or mutated. And actually, more frequently in the right side, there are additional mutations or additional etiological situations in which anti-EGFR antibodies work less.

And so, therefore, if I don't know about a complete molecular profile from these tumors in the right side, I will prefer chemotherapy doublet with bevacizumab. But I should say that if we have a more comprehensive profiling, that we know that all the other potential resistant genes are wild-type, all these biomarkers will tell that also in right-sided tumors, chemotherapy doublet plus the anti-EGFR monoclonal antibody could work as the best treatment option.

Obviously, for doing this, you need a better molecular characterization and better profiling. And maybe this cannot be done in every hospital in everyday practice.

Dr. Seligmann:

Yeah, I agree, and I think it's a continued journey of personalized medicine in this group of patients. And I agree with you again, for some of these RAS wild-type patients on the right side, it's certainly less clear how to optimally manage them, and they do seem a population of unmet need, I would say.

Do you advocate ever giving triplet chemotherapy with an anti-EGFR agent if you're needing a response?

Dr. Ciardiello:

Actually, I don't think so. We have a randomized phase 3 trial called TRIPLETE, in which basically the addition of panitumumab to FOLFOXIRI or FOLFOX was equal in all efficacy in the antitumor activity endpoints.

Dr. Seligmann:

Yeah, I agree completely. I think the preferred treatment would be with doublet chemotherapy and an anti-EGFR agent.

So thank you. That's all that e have time for. I found this discussion very helpful. Thank you, Fortunato.

Announcer:
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