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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Mutational Testing in mCRC: Methods and Data Driving Treatment Selection

Announcer:
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Dr. Ciardiello:

This is CME on ReachMD. I am Fortunato Ciardiello from Naples in Italy, and I have the great pleasure to share with me our thoughts with Dr. Jenny Seligmann from Leeds in the UK.

The first question for you, Jenny, is we know that for applying precision medicine in metastatic colorectal cancer, we need molecular testing for defining which is the subtype of tumor and which is the most appropriate therapy selection.

What do you say about the basic knowledge that practicing physicians should have for treating patients mostly for the key mutations that define therapy?

Dr. Seligmann:

Sure, thank you. So molecular testing is absolutely essential, as far as I'm concerned, for the modern management of a metastatic colorectal cancer patient. In my view, and in the guideline's view, this should be conducted as soon as possible at the point of diagnosis because the results can directly alter first-line therapy.

I would say that I consider the results in a stepwise fashion. So the first alteration I'm very interested in is microsatellite stability. Is your patient MSI-high and maybe suitable for immunotherapy and, certainly, screening for Lynch as well. And then again, thinking about first-line therapy, the other important alterations that you have to be aware of is the mutation status for KRAS and NRAS exon 2, 3, and 4 and BRAF.

This is for a number of reasons, but for the first line, it's so we can select the appropriate patients for anti-EGFR therapies to be added to chemotherapy. As we know, mutations in these genes is a negative predictive biomarker, so it's really important to know that mutation status, preferably before treatment.

BRAF mutation status is really important as well. So not only is BRAF a negative prognostic marker, but also we can identify patients that will be suitable for BRAF-targeted therapy in the second- and third-line setting at the moment.

Dr. Ciardiello:

We know that international guidelines, including the European Society for Medical Oncology guidelines, state that we should measure these mutations.

Obviously, we can use different methods from PCR to Sanger sequencing or to multigene assessment at the same time, what we call next-generation sequencing techniques. And we can do now these measurements also on plasma.

What are your suggestions for clinical practice?

Dr. Seligmann:

So I think that clinicians have what is available to them in reality, and there's a balance between cost, and there's a balance between turnaround time. My preference is for next-generation sequencing on tumor material. This is where all of our evidence-base has been generated at the moment, but I can see many advantages to circulating biomarkers and, actually, the guidelines are now starting to say if tumor material isn't available, then having circulating biomarkers to guide therapy is very relevant. And we're seeing good concordance, and actually, we may be picking up more patients that may not benefit from anti-EGFR agents, so it's a really exciting field to watch.

Dr. Ciardiello:

But this is very important also because sometimes the patient is operated or comes from a different hospital, it's difficult to find the original tissue or the original biopsy, and then liquid biopsy can be a very helpful solution for these patients. But in your experience in UK, how many patients have not tested before first line? How can we convince doctors and payers that this is very important?

Dr. Seligmann:

So I would say that the problems aren't with the patients being tested; the problems are often in the turnaround times. So there's a real want to improve access to personalized medicine and to get good multigene assays. But sometimes the turnaround times can be quite difficult with sending them to a central facility. So that's one struggle that we're having in the UK. Saying that, in the majority of cases, the results will be available before a patient starts first-line therapy.

Dr. Ciardiello:

And this is very good because, at least in Europe now, we are really practicing precision medicine for metastatic colorectal cancer patients before first-line treatment, when the knowledge of these mutations is really needed. Because what we choose in first-line is what can define the fate of the patients, also for the subsequent lines of treatment.

Thank you very much, and I think this has been very helpful and very nice to talk to you, Jenny.

Dr. Seligmann:

Absolutely. Thank you, Fortunato.

Announcer:
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