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Released: 03/31/2025
Valid until: 11/21/2026
Time needed to complete: 55m

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Defining the Standard of Care and Optimal Sequencing in BRAF-Mutant mCRC: Second Line and Beyond

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Ciardiello:

This is a CME activity on ReachMD. My name is Fortunato Ciardiello from Naples in Italy, and it is my pleasure to share our thoughts, together with Dr. Jenny Seligmann from Leeds in the United Kingdom.

The topic will be to talk about a very difficult disease to treat, that is metastatic colorectal cancer with a specific mutation on the BRAF gene that is the V600E mutation.

This is the worst prognostic group, especially if it's an MSS tumor for metastatic colorectal cancer and, therefore, it has been very difficult to treat these patients with very limited therapeutic options. And, therefore, I ask you, Jenny, to summarize what we can do today for these patients.

Dr. Seligmann:

Yeah. So I think you make a very good point. In my view, this remains a population of significant unmet need, and we see in consistent data series that they have a worse prognosis than other molecular subtypes. And this is probably for a variety of reasons, including their available therapies. However, there was a real breakthrough with the BEACON trial.

So the BEACON trial was a phase 3, global, randomized trial. It was conducted in patients with metastatic colorectal cancer with a BRAF mutation who had had at least one prior line of therapy. The main analysis of the trial looked at the comparison of encorafenib and cetuximab compared with standard of care, and what was found was that encorafenib and cetuximab was superior across all efficacy outcomes. The primary endpoint was overall survival, and there was a clinical and statistically significant improvement with 3.5 months' superiority in EC [encorafenib and cetuximab] compared with chemotherapy alone.

So this has been a real landmark trial in this group, and for me, this has really altered the management of these patients. But really still with work to do, I would say.

Dr. Ciardiello:

And a comment on the BEACON trial is that almost 1 out of 5 patients had a major response that is basically tumor shrinkage. It is really important for these patients, also for controlling symptoms, besides the prolongation of survival and prolongation of disease-free progression. Can you comment on that?

Dr. Seligmann:

Yeah. I mean you see it in the trial, you see it with tumor markers, you see it with patients in front of you, and you're right. It really highlighted a real success of personalized medicine that by really targeting the tumor can lead to really meaningful clinical benefits, particularly for patients with symptomatic disease where you really want a response. And we often see those BRAF-mutant patients in those positions.

Dr. Ciardiello:

This is very important. Can you also comment on when to test for the BRAF mutation because we are talking about mostly the best timing for EC, encorafenib plus cetuximab combination, as second line. But do you think that it's better to test before first line or we can do between first and second line?

Dr. Seligmann:

No, absolutely, this knowledge should be had at the start of treatment. I think there's lots of different implications for a BRAF mutation. So number one, you wouldn't use an anti-EGFR agent in the first line. Number two, we see commonly that these patients have rapid progression, following rapid deterioration, following disease progression. So I'm always very vigilant with these patients in first line, so I can progress them very quickly to second line therapy.

So I think it's really important to have all of this information up front. Personally, I advocate using targeted treatment in the second line, rather than leaving it for the third or fourth line. There's quite a steep drop-off of BRAF-mutant patients that will progress through the lines of therapy, and, really, we want to give our most effective therapies as high up in the treatment algorithm as possible.

Dr. Ciardiello:

I fully agree with you. Testing the patients before first line prepares us to also follow very closely the first line because, as you said, patients usually progress very rapidly from first-line chemotherapy standard of care combinations. And so we have to be prepared to treat as soon as possible the patients with this very effective combination therapy.

Thank you very much, Jenny. It has been a pleasure.

Dr. Seligmann:

Absolutely. Thank you.

Announcer:
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