Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/maximizing-outcomes-strategic-approaches-in-metastatic-crc-treatment/36513/

Released: 07/24/2025
Valid until: 11/21/2026
Time needed to complete: 53m

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

Maximizing Outcomes: Strategic Approaches in Metastatic CRC Treatment

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

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Eng:
This is CME on ReachMD, and I'm Dr. Cathy Eng. Here with me today is Dr. Scott Kopetz, friend and colleague.

Let's now talk a little bit about studies looking to optimize treatment for our patients with metastatic colorectal carcinoma utilizing anti-eGFR therapy.

You know, I do want to mention I think it’s very important that you have this pivotal BREAKWATER study, and we always have to think about maintenance therapy, though, with any oxaliplatin-based treatment. So can we just talk a little bit about what would you recommend in this setting following the completion of BREAKWATER for individuals that get past the 4-month mark that are still doing well and that may or may not be developing neuropathy that’s significant or hitting the 6-month mark, even though they don’t have neuropathy but we want to make sure that they come off their oxaliplatin-based therapy. What should we tell our healthcare providers and patients?

Dr. Kopetz:
Yeah, it's been certainly one of the questions that keep coming up and thinking about how do we really best guide that management. Of course, we can reflect back to older studies that have looked at how to optimize maintenance and use of 5-FU and bevacizumab, for example, in maintenance. And so the same question really applies in these others.

So in BREAKWATER, the study was written to continue the 5-FU and the encorafenib and cetuximab, and that really is what led to this prolonged progression-free survival. We don't have direct data about whether you need that 5-FU, but there's really interesting biologic rationale that says there's good synergy between the cytotoxic component and the targeted component. And that really impressive progression-free survival over 12 months for a BRAF population really suggests that there is some durability that's coming from that combination. So that is my recommendation, at least, is to follow the protocol and to keep that 5-FU and encorafenib and cetuximab going.

Dr. Eng:
Going back to a non-BRAF patient, when you have a left-sided tumor and they're getting, let's say, FOLFOX and an anti-eGFR therapy based upon PARADIGM or FOLFIRI-based therapy, what do you do in that setting regarding maintenance treatment?

Dr. Kopetz:
Yeah, it's a great question. And this is something that we talk with the patients about their tolerance overall, but I think we can really reflect back on the wonderful outcome data we see with an eGFR regimen in the wild-type, left-sided patients. And those studies were written with continuing the 5-FU and cetuximab.

There was this ERMES study that was reported out last year that was looking at a FOLFIRI backbone and cetuximab and asking the question about whether or not one should continue the FOLFIRI in that setting. And I think that one, really, the authors' recommendation was that one should treat with FOLFIRI and cetuximab until disease progression in that setting.

But this is an area where I think that it's really evolving. There are a lot of opportunities for personalization with the patient based on their overall tolerance and quality of life.

Dr. Eng:
Yeah. Maybe we should touch upon rechallenge, and that's such a hot topic. So there's a lot of studies recently that we've had—CHRONOS, and we've had PARERE that was presented as well at ASCO—talking about eGFR rechallenge. And I think we should probably just touch upon that.

So the patient has had excellent response to therapy after a while, but as you know, they may develop progression of disease. There appears to be some data that we wait at least greater than 6 months, roughly 8 months or so, and we recheck their RAS status, those patients may still benefit from anti-eGFR therapy.

And I don't know about you, but I am rechecking after a prolonged period of being off the treatment. I think there's several phase 2 studies that are ongoing right now that demonstrate the benefit of the rechallenge. I don't know what your thoughts are on that as well.

Dr. Kopetz:
Yeah, just like you, I'm retreating those patients with an eGFR inhibitor. And I think you really hit the key points, is that we do think that, and the data suggests, that if they still have mutated resistance mechanisms acquired—KRAS/NRAS mutations downstream, or these ectodomain mutations in eGFR—that they may not derive benefit. But in the absence of that, I think there's a lot of great opportunities to improve patient outcomes, as you mentioned.

Dr. Eng:
Well, this has been a great discussion. Our time is up, and once again, thank you so much for listening.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by Agile Education. and is part of our MinuteCE curriculum.

To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.