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<https://reachmd.com/programs/cme/ProactiveAdverseEffectManagementinmCRCImprovingTolerabilitytoOptimizePatientOutcomes/32945/>

Released: 03/31/2025

Valid until: 11/21/2026

Time needed to complete: 35m

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## Proactive Adverse Effect Management in mCRC: Improving Tolerability to Optimize Patient Outcomes

### 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. I am Fortunato Ciardiello, and today I am together with Dr. Jenny Seligmann.

We will talk now about side effects, tolerability, and the management of treatment with one anti-EGFR agent, cetuximab, and one anti-BRAF mutant agent, that is encorafenib. It is very important to know them and manage them because they are very different from the classical chemotherapy side effects.

And so, Jenny, first question is, can you just recap: Which are the classical toxicity of these agents and, mostly, their frequency and how we can manage them?

### Dr. Seligman:

Yeah. I think part of the complexity here is that the 2 agents have quite a lot of overlapping toxicity. If we look back to the data from the BEACON trial, the most frequently reported adverse events were diarrhea, nausea, anorexia, and cutaneous toxicity. And what they found in BEACON was that, actually, it didn't lead to a huge amount in the way of dose reduction and very few treatment cessations.

And what's really important is that all members of the multidisciplinary team who may be seeing the patients should be aware of the types of toxicity that these patients may have and that they're different from chemotherapy, indeed, and that the algorithms for managing them are very clear. So your nurse prescribers, your pharmacists, etc. But really critically, I think you need to speak to the patients very carefully about the type of toxicity. For example, cutaneous toxicity is very common with both of these drugs. They both cause slightly different cutaneous toxicity, but some overlap. And what I'm very careful to tell my patients is, it's much easier to manage a grade 1 rash than it is to manage a grade 3 rash, so we would encourage patients to come forward and tell us about these troubles that they're having.

A lot of patients are worried that you're going to stop the medication, but actually, you can give them reassurance that most of the cutaneous toxicity is easily managed. A lot of it won't result in a dose reduction.

### Dr. Ciardiello:

In your practice, how often you have to stop both drugs because they cannot be managed without a side effect? Is that rare or something that can happen often?

### Dr. Seligmann:

I haven't stopped one patient on encorafenib and cetuximab due to side effects as yet. I have dose-reduced some patients, and

particularly for cetuximab-related rashes, I've had interruptions in their treatment. But mainly I've been able to restart, sometimes at a lower dose, particularly more with the encorafenib. Occasionally, particularly when we started using the drugs, we needed the help of our dermatology colleagues, and I think, looking back a few years ago, I was more inclined to interrupt and send to dermatology, whereas now, with medical photography, it's quite easy, and I feel happier managing these drugs now. And actually, it's quite rare that you dose-reduce compared with some other regimens that we use in oncology.

**Dr. Ciardiello:**

And it's also very important to highlight that encorafenib plus cetuximab should be given together because, basically, as a single-treatment monotherapy, they are not effective at all. So basically, it's better to do a dose reduction that allows to keep on with the treatment or even to stop both drugs for a short time and then we start together. But we cannot say let's stop encorafenib and keep on going with cetuximab or vice versa because we know that single agent do not work in these patients.

**Dr. Seligmann:**

Yeah, I agree completely. And I think the way that I manage this now is to have a very proactive approach with patients at the start. This is an effective drug, and what we want to do is maintain the treatment intensity as much as possible. So anything that the patients can do beforehand to try and reduce the chances of them developing rash. So very simple skin care advice regarding sunscreens and staying out of direct sunlight, showering with nonirritant body wash, even diet. Sometimes patients are more likely to have diarrhea; sometimes modifying their diet can help. But I think we should be really encouraging proactive management of the toxicity to try and continue patients on the drug, particularly if they're having a good symptomatic, radiological, and biomarker result from the treatment.

**Dr. Ciardiello:**

Thank you very much. This is very helpful and I think very informative for our physicians.

**Dr. Seligmann:**

Thank you very much.

**Announcer:**

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