# Less chemotherapy may have more benefit in rectal cancer

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Christopher Lieu, MD. Credit: CU Anschutz Medical Campus

Chemotherapy used to shrink a tumor before surgery, called neoadjuvant chemotherapy, is becoming more common in many cancers, including stage II and III rectal cancer. However, the chemotherapy regimens FOLFOX and CapeOx used in this setting come with significant side effects, to the degree that many patients are unable to complete the recommended schedule.

Now a University of Colorado Cancer Center study presented at the 2020 Gastrointestinal Cancers Symposium shows they may not have to: A small study of 48 patients with locally advanced rectal cancer

receiving neoadjuvant chemotherapy, found that patients receiving lower-than-recommended doses in fact saw their tumors shrink more than patients receiving the full dose.

"I think we need bigger studies to explore less intensive therapy—maybe lower doses, maybe a shorter course of treatment—to see what is the optimal dosing prior to surgery," says Ashley E. Glode, PharmD, assistant professor at the Skaggs School of Pharmacy and Pharmaceutical Sciences, and the study's first author.

In some cancers, a tumor may be entwined with nearby organs and blood vessels to the point that surgery is not initially an option. Most patients with locally advanced rectal cancer are surgical candidates, but chemotherapy used to shrink a tumor prior to surgery has been associated with more successful surgeries and a lower rate of cancer recurrence. As a high-volume center for the treatment of these cancers, University of Colorado Cancer Center oncologists including Christopher Lieu, MD, noticed that patients who were unable to complete the recommended course of neoadjuvant chemotherapy seemed to have similar or even better outcomes than patients receiving the full dose, prompting the current study.

"We do all sorts of supportive care options to help keep patients on these therapies at the recommended, high doses. But based on our observations and on this early study, we're starting to talk about having less hesitancy to drop the drug or at least decrease the dosing," says Lieu, who is CU Cancer Center's interim associate director for clinical research.

Of the 48 patients included in the study, only 12.5 percent were able to tolerate the full dose of chemotherapy. Due to side effects, zero of six patients taking the regimen CapeOx completed the recommended dose.

"CapeOx is a treatment option mostly taken at home as a pill so it's

easier for patients—they only have to come in for infusion once every three weeks. But the regimen wasn't tolerated by any patients on this study. It makes us think about not offering the option of CapeOx, and sticking with FOLFOX instead," Glode says.

In 42 patients receiving less than the full dose of FOLFOX, 45 percent experienced a complete response, meaning that cancer was undetectable after treatment (negating the need for surgery in eight cases). In 6 patients receiving the full dose of FOLFOX, 33 percent experienced a complete response.

"This is a small, single-institution study, but it certainly gives us pause," Glode says. "Why would patients take more chemotherapy and have more side effects, when less chemotherapy seems equally or even more beneficial?"

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