

Identifying colorectal cancer subtypes could lead to improved treatment decisions

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Heinz-Josef Lenz, MD. Credit: Ricardo Carrasco III, Keck Medicine of USC

Colorectal cancer is the second leading cause of cancer death in the U.S., expected to cause about 51,000 deaths in 2019. But until now, it was unclear which drugs were most effective for which patients.

Researchers at the USC Norris Comprehensive Cancer Center found that

identifying a metastatic [colorectal cancer](#) patient's Consensus Molecular Subtype (CMS) could help oncologists determine the most effective course of treatment. CMS also had [prognostic value](#), meaning each subgroup was indicative of a patient's overall survival, regardless of therapy. The results are from the multi-center Phase III CALGB/SWOG 80405 trial and published in the *Journal of Clinical Oncology*.

CMS categorizes colorectal [cancer](#) into four distinct, biologically characterized subgroups based on how mutations in the tumor behave. The subgroups were created using data from several research teams around the world that had previously analyzed tumors of colorectal cancer [patients](#) who were treated with surgery and adjuvant chemotherapy. Although CMS classification is not based on clinical outcomes, there seemed to be patterns in how different subtypes responded to treatment.

"We wanted to understand the importance of CMS for patients with metastatic disease who are treated with the two most important first-line therapies," says Heinz-Josef Lenz, MD, Professor of Medicine in the Division of Oncology at the Keck School of Medicine of USC and J. Terrence Lanni Chair in Gastrointestinal Cancer Research at USC Norris. Lenz was the lead author on the study. "We anticipated that CMS had prognostic value, but we were impressed at how strongly CMS was associated with outcomes."

The study compared the efficacy of two different therapies (chemotherapy and cetuximab versus bevacizumab) on 581 metastatic colorectal cancer patients categorized by CMS. The data showed a strong association between a patient's CMS subtype and both overall survival and progression-free survival. For example, patients in CMS2 had a median overall survival of 40 months compared to 15 months for patients in CMS1.

CMS also was predictive of [overall survival](#) among patients on either treatment, with patients in certain subtypes faring better on one therapy over the other. Survival for CMS1 patients on bevacizumab was twice that of those on cetuximab, whereas survival for CMS2 patients on cetuximab was six months longer than for bevacizumab.

"This study establishes the clinical utility of CMS in treating colorectal cancer," Lenz says. "It also provides the basis for more research to uncover additional clinically significant predictive signatures within these subtypes that might better personalize [patient care](#)."

Currently, it is not possible to order patient subtyping, though multiple efforts are underway to develop an assay approved for clinical use. Lenz estimates that this could happen in a matter of months. Until then, he and his colleagues continue to analyze data from more than 44,000 samples of blood, tissue and plasma in one of the largest, most comprehensive research efforts to characterize DNA, RNA and germline DNA in colon cancer. "This is only one study of many more to come that will help us understand this disease at the molecular level so we can provide better care for patients," Lenz says.

More information: Heinz-Josef Lenz et al, Impact of Consensus Molecular Subtype on Survival in Patients With Metastatic Colorectal Cancer: Results From CALGB/SWOG 80405 (Alliance), *Journal of Clinical Oncology* (2019). [DOI: 10.1200/JCO.18.02258](https://doi.org/10.1200/JCO.18.02258)

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