

Colorectal cancer patients with gene mutation show better response to cancer agent

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Even though the cancer-treatment agent cetuximab is not considered effective treatment for KRAS (a gene)-mutated metastatic colorectal tumors, new research indicates that patients with colorectal cancer not responding to chemotherapy and a certain variation of this gene who were treated with cetuximab had longer overall and progression-free survival than patients with other KRAS-mutations, according to a study in the October 27 issue of *JAMA*.

"Recent retrospective correlative analyses of metastatic colorectal cancer trials indicate that patients with KRAS-mutated tumors do not benefit from the anti-epidermal [growth factor receptor \(EGFR\) monoclonal antibodies cetuximab](#) and panitumumab," the authors write. However, they add there are indications that not all KRAS mutations are equal in their biological characteristics, including anecdotal reports indicating that a minority of patients with KRAS-mutated tumors can respond to anti-EGFR therapy.

Wendy De Roock, M.D., of the University of Leuven, Leuven, Belgium, and colleagues conducted a study to examine whether a certain KRAS mutation (p.G13D) may be associated with a better outcome after cetuximab treatment than observed with other KRAS mutations. The study included a pooled data set of 579 patients with chemotherapy-refractory (not responsive to treatment) colorectal cancer treated with cetuximab between 2001 and 2008 and who were included in other clinical trials or received off-study treatment. Various analyses of the data were performed. The main efficacy outcome measure was overall survival; secondary efficacy measures were response rate and progression-free survival.

The researchers found that among patients who

received any cetuximab-based treatment (cetuximab [monotherapy](#) or cetuximab plus chemotherapy) (n = 571), overall and progression-free survival were significantly longer in patients with p.G13D-mutated tumors (overall survival: n=32; median [midpoint], 7.6 months; progression-free survival, n = 32; median, 4.0 months) than in patients with other KRAS-mutated tumors (overall survival: median, 5.7 months; progression-free survival: median, 1.9 months).

"In a large, retrospective pooled exploratory analysis of patients with chemotherapy-refractory [colorectal cancer](#), we show for the first time that there is a positive association between KRAS p.G13D mutations and cetuximab treatment in regard to better overall and progression-free survival," the authors write. They add this effect may not be due to a real reduction in tumor burden but to a delay in progression.

"Prospective randomized trials are needed before conclusions about potential beneficial effects of cetuximab in p.G13D-mutated chemotherapy-refractory metastatic colorectal [cancer](#) should be inferred."

More information: *JAMA*. 2010;304[16]:1812-1820.

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