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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.