TUMOR GENOTYPING
TO PREDICT RESPONSE

Mutations in *KRAS* confer resistance to anti-EGFR therapy. Patients with metastatic colorectal cancer (mCRC) are, therefore, profiled for seven *KRAS* mutations before receiving cetuximab or panitumumab. In a study published in the *Lancet Oncology*, primary tumor samples ($n = 773$) were collected from patients with chemotherapy-refractory mCRC treated with cetuximab. The effects of *KRAS*, *BRAF*, *NRAS*, and *PIK3CA* mutations on the efficacy of cetuximab plus chemotherapy were evaluated. "We used a centralized and advanced mutation detection technology to ensure that all samples were analyzed by the same method, that the number of potentially occurring mutations assessed were maximized, and high sensitivity meant our analysis was not affected by the quality of the tumor samples," says lead investigator Sabine Tejpar.

Objective response was the primary end point, and progression-free survival and overall survival were secondary end points. Multivariate analyses confirmed significant associations between outcome and *KRAS*, *PIK3CA* exon 20, *NRAS* and *BRAF* mutation status. "Our results provide a clear picture of the efficacy of cetuximab plus chemotherapy in chemotherapy-refractory mCRC according to the presence or absence of activating mutations in these genes," says Tejpar.

Samples were retrospectively genotyped so the prognostic or true predictive effects could not be determined. Also, this information will have to be weighed against the cost and feasibility of genotyping tumor samples prior to therapy. However, "advances in genotyping assays, preferably dedicated drug-specific multiplex assays combining positive and negative molecular predictors, are within our reach and will provide the necessary advance for true personalized medicine," concludes Tejpar.

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Original article De Roock, W. *et al.* Effects of *KRAS*, *BRAF*, *NRAS*, and *PIK3CA* mutations on the efficacy of cetuximab plus chemotherapy in chemotherapy-refractory metastatic colorectal cancer: a retrospective consortium analysis. *Lancet Oncol.* 11, 753–762 (2010)