K-ras
Mutation Analysis

For **metastatic colorectal cancer** prognosis and therapy evaluation

Survival rates for patients with metastatic colorectal cancer (mCRC) have increased significantly in recent years, mainly due to the use of new combinations of existing chemotherapies and the introduction of targeted therapies.[1]

These therapies, which often target key cell signaling pathways such as those influenced by the epidermal growth factor receptor (EGFR), may require laboratory testing for patient stratification to identify which individuals are more likely to respond. Targeted therapies include those that utilize monoclonal antibodies against EGFR (cetuximab, panitumumab), as well as small molecule tyrosine kinase inhibitors.

Many cancer therapies are associated with increased toxicity, and clinical response and drug resistance varies among patients.[1] Being able to identify which patients may benefit from certain therapies provides important clinical information to assist physicians in recommending and assessing treatment regimens.

Mutations in the k-ras oncogene are common among patients with colorectal cancer.[1] Recent studies have demonstrated that k-ras mutation status is associated with patient prognosis and predictive of potential response to therapy.[1-2] The overall survival of patients without a k-ras mutation in their tumor sample, and who received monoclonal antibody-based therapy, was significantly higher compared to patients with a tumor containing mutated k-ras.[1]

Analysis of the k-ras gene for mutation status has been shown to be a predictive clinical biomarker that can help stratify patients with mCRC who are more likely to respond to treatment with cetuximab (Erbitux®) or panitumumab (Vectibix™).[1-4]

Patient Response to Panitumumab Therapy[4]

	Patients With Response to Panitumumab	Patients with Stable Disease on Panitumumab
Nonmutated (wild type) k-ras	17%	34%
Mutated k-ras	0%	12%

Patients with a nonmutated k-ras who received panitumumab (Vectibix™) therapy responded positively and displayed longer progression-free survival than patients who have the k-ras mutation.[3-4]

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K-ras Mutation Analysis

K-ras Gene Mutation Detection 480090

CPT 83891; 83896(x8); 83898(x8); 83907; 83912

Special Instructions Please provide a copy of the pathology report. Please direct any questions regarding this test to customer service at 800-533-0567.

Specimen Formalin-fixed, paraffin-embedded (FFPE) tissue

Volume Five precut, unstained slides from paraffin block in 10-µm sections, and one H&E reference slide or formalin-fixed, paraffin-embedded tissue block containing ≥50% tumor.

Minimum Volume 2 mm x 2 mm tumor area

Container Slides, blocks

Collection Please provide five unstained slides and one H&E-stained slide at 10 µm or a tissue block.

Storage Instructions Maintain blocks and slides at room temperature.

Causes for Rejection Tumor block containing insufficient tumor tissue or tumor fixed in a heavy metal fixative; broken or stained slides.

Use Mutations in the k-ras oncogene are frequently found in human cancers. They are common in pancreatic cancer, colorectal cancer, lung adenocarcinoma, gall bladder cancer, bile duct cancer, and thryoid cancer. These mutations may indicate prognosis and drug response and many new cancer therapies are being targeted to the k-ras pathway. This assay detects seven k-ras mutations in codons 12 and 13, allowing determination of whether there is a correlation between k-ras mutation status and drug response.

Limitations The provided tumor tissue should be composed of ≥50% tumor cells for accurate test interpretation. Preparation of DNA from tissue samples is dependent on the quality of the specimen provided. Inadequate DNA extraction may occur in a significant number of paraffin-embedded samples. The methods used in this assay are highly selective and, depending on the total amount of DNA present, can detect approximately 1% of mutant in a background of wild-type genomic DNA. The assay has a limit of detection of between 5 and 10 copies.

Methodology Amplification refractory mutation system (ARMS) and real-time polymerase chain reaction using Scorpions™ technology

References

1. Lièvre A, Bachet JB, Le Corre D, et al. KRAS mutation status is predictive of response to cetuximab therapy in colorectal cancer. *Cancer Res.* 2006 Apr 15; 66(8):3992-3995.

2. Sartore-Bianchi A, Moroni M, Veronese S, et al. Epidermal growth factor receptor gene copy number and clinical outcome of metastatic colorectal cancer treated with panitumumab. *J Clin Oncol.* 2007 Aug 1; 25(22):3238-3245.

3. Freeman D, Juan T, Meropol NJ, et al. Association of somatic KRAS gene mutations and clinical outcome in patients with metastatic colorectal cancer (mCRC) receiving panitumumab monotherapy. *Eur J Cancer.* 2007; 5(4):suppl:239.

4. Amado RG, Wolf M, Freeman D, et al. Analysis of KRAS mutations in patients with metastatic colorectal cancer receiving panitumumab monotherapy. *Eur J Cancer.* 2007; 5(6):suppl:8.

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