

KRAS Mutation Detection in Colorectal Cancer

FOR DETERMINING MUTATIONAL STATUS THAT CONFERS RESISTANCE TO ANTI-EGFR THERAPY.

Disease Overview

- In the United States, colorectal cancer is the third most common form of cancer; individuals have a 6 percent lifetime risk of developing this disease.
- Most colorectal cancer is caused by somatic mutations and is not hereditary.
- Mutations in the oncogene *KRAS* are seen in 30–40 percent of sporadic colorectal cancers.

Indications for Ordering

- *KRAS* mutations in codons 12 and 13 have been linked with resistance to anti-EGFR therapy in metastatic colorectal cancer.
- Patients should be tested for *KRAS* mutations prior to undergoing treatment with anti-EGFR therapies, such as cetuximab (Erbix[®]).

Interpretation

The presence of an oncogenic mutation in codon 12 or 13 of *KRAS* is indicative of resistance to anti-EGFR therapies.

Methodology

- Tumor tissue is microdissected and DNA extracted from five micron sections of formalin-fixed paraffin-embedded tissue blocks.

- A region covering codons 12 and 13 of the *KRAS* gene is amplified using polymerase chain reaction (PCR), followed by pyrosequencing.

Limitations

Mutations in other locations within the *KRAS* gene or in any other gene will not be detected.

Clinical and Analytical Sensitivity

- All 12 potentially oncogenic mutations in codons 12 and 13 are detected.
- Limit of detection for this assay is 10 percent mutant alleles.

References

1. Di Fiore F, et al. Clinical relevance of *KRAS* mutation detection in metastatic colorectal cancer treated by Cetuximab plus chemotherapy. *Br J Cancer* 2008;99:551–2.
2. Lievre A, et al. *KRAS* mutation status is predictive of response to cetuximab therapy in colorectal cancer. *Cancer Res* 2006; 66:3992–5.
3. Lievre A, et al. *KRAS* mutations as an independent prognostic actor in patients with advanced colorectal cancer treated with cetuximab. *J Clin Oncol* 2008;26:374–9.
4. Ogino S, et al. Sensitive sequencing method for *KRAS* mutation detection by Pyrosequencing. *J Mol Diagn* 2008; 7:413–21.

Test Information

0040248

KRAS Mutation Detection

For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult[®] at www.arupconsult.com.