

# KRAS Mutation Detection in Colorectal Cancer

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

### Test Highlights

- Includes detection of mutations in *KRAS* codons 12, 13, and 61.
- *KRAS* mutation testing with reflex to *BRAF* mutation testing is also available.

### 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 approximately 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. *KRAS* mutations in codon 61 may also confer resistance to anti-EGFR therapy.
- Patients should be tested for *KRAS* mutations prior to undergoing treatment with anti-EGFR therapies, such as cetuximab (Erbbitux<sup>®</sup>).

### Interpretation

- The presence of an oncogenic mutation in *KRAS* is indicative of resistance to anti-EGFR therapies.
- There is recent evidence suggesting susceptibility to anti-EGFR therapies in tumors harboring the p.Gly13Asp mutation.

### Methodology

- Tumor tissue is microdissected and DNA extracted from five micron sections of formalin-fixed, paraffin-embedded tissue blocks.
- Regions covering codons 12, 13, and 61 of the *KRAS* gene are amplified using polymerase chain reaction (PCR). Mutation status is determined by pyrosequencing.

- All potentially oncogenic mutations in codons 12, 13, and 61 are detected.
- Limit of detection for this assay is 10 percent mutant alleles.

### Limitations

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

### References

1. De Roock W, et al. Association of *KRAS* p.G13D mutation with outcome in patients with chemotherapy-refractory metastatic colorectal cancer treated with cetuximab. *JAMA* 2010;304:1812-20.
2. 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.
3. Lievre A, et al. *KRAS* mutation status is predictive of response to cetuximab therapy in colorectal cancer. *Cancer Res* 2006;66:3992-5.
4. 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.
5. Loupakis F, et al. *KRAS* codon 61, 146 and *BRAF* mutations predict resistance to cetuximab plus irinotecan in *KRAS* codon 12 and 13 wild-type metastatic colorectal cancer. *Br J Cancer* 2009;101:715-21.
6. 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

2001932

*KRAS* Mutation Detection with Reflex to *BRAF* Codon 600 Mutation Detection

For specific collection, transport, and testing information, refer to the ARUP website at [www.aruplab.com](http://www.aruplab.com).

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

### AUTHORS

Wade Samowitz, MD

Cecily Vaughn, PhD