

Assay Summary

Somatic KRAS Genotyping KRAS Gene, 7-Mutation Analysis

Synopsis

KRAS somatic mutations are found in 30-40% of colorectal cancer's (CRC)^{1,2} and 10-30% of non-small cell lung carcinomas (NSCLC)³. Mutations have been reported in codons 12, 13, and 61, but a majority of these consist of six mutations in codon 12 (gly12ala, gly12asp, gly12arg, gly12cys, gly12ser, and gly12val) and one in codon 13 (gly13asp). Tumors with these mutations have been associated with poor responsiveness to anti-EGFR therapies^{2,4-6}.

Determining the KRAS status of a newly diagnosed NSCLC or CRC patient prior to initiating anti-EGFR therapy could be useful in selecting candidates for tyrosine kinase inhibitor (TKI) and monoclonal antibody (MAB) therapy, respectively. Additionally, testing could be considered for these individuals who are already on anti-EGFR therapy, but are demonstrating resistance.

Indications for testing

Individuals with a new diagnosis of CRC or NSCLC prior to initiating anti-EGFR therapy, or a history of CRC or NSCLC and demonstrated resistance to anti-EGFR therapy.

Methodology

Mutation analysis of the KRAS gene: A PCR based fragment analysis using "Shift Termination" technology which recognizes wild type or mutant target sequences and selectively extends detection primers with 1 to 20 labeled nucleotides has been optimized and validated by the Molecular Diagnostic Laboratory (MDL). We specifically test codons 12 and 13 for the following mutations: gly12ala, gly12asp, gly12arg, gly12cys, gly12ser, gly12val, gly13asp, gly13ser, gly13arg, gly13cys, gly13ala, and gly13val. Testing is performed on micro-dissected cells from formalin fixed, paraffin embedded tissue.

Performance

The sensitivity of this assay can detect down to 5 in 100 mutation-bearing cells in a micro-dissected area. This method will not detect mutations other than the ones listed above.

Specimen Requirements

Mutation analysis of the KRAS gene: Send 6 slides of tumor sample (5 micron serial sections, unstained; 1 H/E stained). Ensure that the slides are clearly labeled with the patient name or identifier and date of birth and type of sample. Place slides in appropriate containers to ensure against breakage. Alternatively, the paraffin blocks may be submitted. Please include a copy of the Pathology report.

Test Request Form (TRF)

A completed MDL [TRF](#) is required for each specimen. Please submit the completed TRF with the specimen. Complete testing and billing information must be provided before the specimen is processed.

| <i>Order Codes</i> | <i>CPT Codes</i> | <i>TAT</i> |
|---|---|-------------------|
| KRAS-T (KRAS gene, mutation analysis of codons 12 and 13) | 83890, 88323, 88381, 83892, 83898(x7), 83909, 83912 | 1 wk |

References

1. Lièvre, A. et al., (2008) J Clin Oncol; 26:374-9
2. Amado, R. G. et al., (2007) Eur J of Can Supp (5):6
3. Eberhard et al. (2005) J Clin Oncol; 23:5900-9
4. Di Fiore, F. et al., (2007) Br J Cancer; 96:1166-9
5. Han. et al., (2006) Clin Can Res; 12:2538-44
6. Pao. et al., (2005) PLoS Med; 2:e17

NOTE: This test is performed pursuant to a license agreement with Roche Molecular Systems, Inc.