KRAS and BRAF Mutation Spectrum In 1,035 FFPE Tumor Samples Submitted For Clinical Testing

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Introduction

Activating mutations in both the KRAS and BRAF genes are associated with poor prognosis and non-response to anti-EGFR therapies in patients with advanced cancers. Clinical guidelines have recommended that KRAS mutational status be determined in all patients with metastatic colorectal cancer that are being considered for anti-EGFR therapies. In this study, a pathologist reviewed an H&E slide of each tumor sample and determined the percent tumor nuclei and percent necrosis. Each specimen was macrodissected and DNA was extracted. DNA was then amplified with primers flanking KRAS exon 2 (codons 12 and 13), and KRAS exon 3 (codon 61), and BRAF exon 15. Using the ABI3730 and Mutation Surveyor software, mutations were scored as positive when evident in both the forward and reverse reactions. A total of the 1,035 clinical tumor specimens were submitted to our lab for KRAS and/or BRAF mutation analysis by direct sequencing or PCR analysis.

Results

KRAS and BRAF in α-EGFR Antibody Resistance

Mutation Spectrum of Samples Tested for KRAS

KRAS Mutations in Different Tumor Types

Conclusions

- ~40% of colorectal samples were positive for KRAS mutations
- The most common mutation observed in KRAS was p.G12D
- 4.6% of all mutations observed in KRAS occurred in codon 61
- Testing for the 7 most common KRAS variants would have a clinical sensitivity of 94%
- V600E mutations in BRAF comprised ~93% of all mutations observed in exon 15
- Two rare variants were observed in exon 15 of BRAF (p.V600R and p.V600K) in skin samples
- ~10% of colon cancer samples and ~60% of skin samples were positive for BRAF

References: