

Clinical Report for Mutation Testing Service

PATIENT AND ORDER INFORMATION	
Name: WILLIAMSON, ADAM DoB: 11 Mar 1945 Age: 66 Sex: Male Biopsy Site: Colon Specimen Collected: 10 Dec 2011 Specimen Received: 13 Dec 2011	Pathwork Case ID: MOL11-000006 Test Report Date: 17 Dec 2011 Specimen ID: C-25-6543 1A
TREATING PHYSICIAN	SUBMITTING PHYSICIAN
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MUTATION TEST RESULTS

TEST PERFORMED	RESULT (Positive or Not Detected)	MUTATION DETECTED
KRAS BRAF	NOT DETECTED POSITIVE	— V600E

INTERPRETATION & REFERENCES

KRAS gene is mutated in approximately 40% of colorectal cancers (CRC), and mutations are associated with resistance to anti-epidermal growth factor receptor (anti-EGFR) targeted therapies. Clinical practice guidelines from American Society for Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN) have recommended KRAS mutation testing at codons 12 and 13 for all patients with metastatic CRC being considered for anti-EGFR monoclonal antibody therapy, such as cetuximab or panitumumab.

BRAF gene is mutated in 10 – 17% of colorectal cancers. Studies have shown patients who have colorectal carcinoma with a BRAF V600E mutation appear to have a poorer prognosis, and show resistance to anti-EGFR antibody therapy. BRAF and KRAS are generally not found in the same tumors. The NCCN recommends that patients who test positive for wild-type (non-mutated) KRAS be considered for BRAF testing.

ASCO Provisional Clinical Opinion. J Clin Onc. 2009 27: 2091-2096
 Fiore, et al. Br J Can 2008 99:551-552
 Wang, et al. Adv Anat Path 2010 17:23-32
 Benvenuti, et al Cancer Res 2007 67:2643-2648
 NCCN Guidelines Ver 2.2012 Colon Cancer
 Di Nicolantonio et al. J Clin Onc 2008 26:5705-12, 2008
 Laurent-Puig et al. J Clin Onc 2009 vol. (35): 5924-5930

TEST METHOD DESCRIPTION

Prior to DNA extraction, submitted tissues are reviewed by a pathologist and tumor areas are selected for microdissection, if needed, to enrich for tumor cells. All DNA samples are assessed for adequacy by real-time PCR assay utilizing Amplification Refractory Mutation System (ARMS) and Scorpions technology prior to mutation testing. The KRAS test can detect the presence of seven common mutations (Gly12Ala, Gly12Asp, Gly12Arg, Gly12Cys, Gly12Ser, Gly12Val, and Gly13Asp) found in codons 12 and 13 of the KRAS oncogene. The level of detection for all KRAS mutations is between 1 – 5% against a background of wild-type genomic DNA. The BRAF test can detect the presence of V600E mutation (1799T>A), and will also detect V600E (1799_1800TG>AA) complex and V600D (1799_1800TG>AT) complex, but will not distinguish between them. All the mutations are found in exon 15 of the BRAF oncogene. The level of detection for all BRAF mutations is 1% against a background of wild-type genomic DNA.

Estimated Percent Tumor Tissue in Sample Tested: _____ % Comment: _____

CLIA Number: 05D1080859

Laboratory Director: Meredith Halks Miller, M.D.

The performance characteristics of this test were determined by Pathwork Diagnostics Laboratory. This test has not been approved by the US Food and Drug Administration. This laboratory is CAP accredited and regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as certified to perform high complexity clinical testing. This assay is used for clinical purposes and the results should be interpreted in reference to other laboratory and clinical findings.