

Clinical Report for Mutation Testing Service

PATIENT AND ORDER INFORMATION

Name: WALTERS, ABIGAIL	Pathwork Case ID: MOL11-000004
DoB: 03 Ap 1933 Age: 78 Sex: Female	Test Report Date: 11 Dec 2011
Biopsy Site: Bronchus	Specimen ID: N-11-168324 2A & 2B
Specimen Collected: 05 Dec 2011	
Specimen Received: 08 Dec 2011	

TREATING PHYSICIAN	SUBMITTING PHYSICIAN
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MUTATION TEST RESULTS

TEST PERFORMED	RESULT (Positive or Not Detected)	MUTATION DETECTED
EGFR KRAS	NEGATIVE POSITIVE	— Gly12Arg (<u>GGT</u> > <u>CGT</u>)

INTERPRETATION & REFERENCES

EGFR mutations occur in approximately 10% of Caucasian patients and up to 50% of Asian patients with non-small cell lung cancer (NSCLC), and have been correlated with response to EGFR tyrosine kinase inhibitors (TKI), such as erlotinib and gefitinib. Conversely, T790M mutation has been shown to result in acquired EGFR TKI resistance in patients with recurring NSCLC who have been previously treated with TKI therapy. Clinical practice guidelines from the American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN) recommend EGFR mutation testing prior to initiation of anti-EGFR TKI therapies.

The presence of KRAS mutations is prognostic of poor survival for patients with NSCLC, when compared to the absence of KRAS mutations, independent of therapy. KRAS mutations may also be associated with intrinsic TKI resistance.

Mok, et al. N Engl J Med 2009 361:947-957
 Bean, et al. PNAS 2007; 104:20932-20937
 Miller, et al. J Clin Onc 2008 26:1472-1478

Riely et al. Proc Am Thorac Soc 6(2):201-205
 NCCN Guidelines Ver 2.2012 Non-Small Cell Lung Cancer
 Ladanyi, et al. Mod Path 2008 21:S12-S22

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 EGFR test detects 7 mutations, 3 insertions, and 19 deletions. Note G719A, G719S, and G719C mutations can be detected, but not distinguished, so if present are reported as G719X. The exon 19 deletions and exon 20 insertions can also be detected, but not distinguished. The level of detection for all EGFR mutations is 1 – 2% against a background of wild-type genomic DNA. The table below lists all mutations detectable by this assay.

Mutations:	T790M, 2369C>T, exon 20	L858R, 2573T>G, exon 21	L861Q, 2582T>A, exon 21	S768I, 2303G>T, exon 20	G719A, 2156G>C, exon 18	G719S, 2155G>A, exon 18	G719C, 2155G>T, exon 18
Insertions, all on exon 20	2307_2308ins9	2319_2320insC AC	2310_2311insG GT				
Deletions, all on exon 19	2235_2249del1 5	2235_2252>AA T (complex)	2236_2253del1 8	2237_2251del1 5	2237_2254del1 8	2237_2255>T (complex)	2236_2250del1 5
	2238_2255del1 8	2238_2248>GC (complex)	2238_2252>GC A (complex)	2239_2247del9	2239_2253del1 5	2239_2256del1 8	2239_2248TTA AGAGAA>C (complex)
	2239_2258>CA (complex)	2240_2251del1 2	2240_2257del1 8	2240_2254del1 5	2239_2251>C (complex)		

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.

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.

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