Rosetta Genomics, Inc.
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Philadelphia, PA 19104 USA
US Toll Free☎: 1-888-522-7971 ☎: 1-215-382-9000
Fax: 1-215-382-0815 www.rosettagenomics.com CLIA ID 39D1090331

Patient Information

Name: John Smith
DOB: 01/02/1930 Age: 85
Sex: Male
Address: 111 Any Street
Any Town, NJ

Ordering Physician

Name: Dr. Oncologist, MD
Account: Oncology Practice
Address: 123 Any Street
Any Town, NJ
Phone: 123-456-7890
Fax: 098-765-4321

Copy To (If different from ordering)

Name: Dr. Pathologist, MD
Account: Pathology Practice
Address: 321 Any Street
Any Town, NJ
Phone: 987-654-3210
Fax: 135-791-1131

Sample Information

Date Collected:	06/23/2015	Specimen Type:	FFPE Slides	Barcode #:	Sample #:
Date Received:	08/06/2015	Date of Report:	08/14/2015	Submitting Lab ID #:	

Tumor Profile for John Smith

ICD-10: C34.90 Malignant neoplasm of unspecified part of unspecified bronchus or lung

OncoGxLung™ NGS Report
Rosetta Genomics in partnership with Admera Health

KEY FINDINGS

Potential clinical benefit with **Gefitinib**, **Erlotinib**, **Afatinib**, **Dacomitinib**, **AZD-9291** due to EGFR E746_A750del.

**The Key Findings section is an overview of potential therapeutic benefit or lack thereof. Please refer to the information below for details.*

Medically Actionable Alterations

Therapies With Potential Clinical Benefit				
Gene	**Mutation Detected**	**Therapies**	**Tumor Type**	**Reference**
EGFR	E746_A750del	Gefitinib, Erlotinib, Afatinib	Non-Small Cell Lung Cancer	FDA drug label
EGFR	E746_A750del	Dacomitinib	Non-Small Cell Lung Cancer	Ramalingam, et al. 2012
EGFR	E746_A750del	AZD-9291	Non-Small Cell Lung Cancer	Jänne, et al. 2015

Therapies With Potential Lack of Clinical Benefit in the Patient's Tumor Type				
Gene	**Mutation Detected**	**Therapies**	**Tumor Type**	**Reference**
No medically actionable mutations were detected in this category.				

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Alteration Details with Therapeutic Implications by Tumor Type

EGFR	
Gene: EGFR Nucleotide: c.2235_2249del15	**Pathways: EGF/EGFR Signaling**
Alteration Detected: E746_A750del	**Variation Type: Deletion**
Response to Gefitinib, Erlotinib, Afatinib, Dacomitinib, AZD-9291:	➢ **Increased efficacy in Non-Small Cell Lung Cancer**

Genes with medically actionable alterations are shown above. No alterations of known clinical significance were detected in the remainder of the OncoGxLung Panel Genes shown in Table 1.

Clinical Trials to Consider

***EGFR* Associated Clinical Trials**				
Therapies	**NCT ID**	**Title**	**Phase**	**Locations#**
Afatinib	NCT02514174	A Single Arm Phase IV Study of Afatinib in Elderly Patients With Stage IV or Recurrent Non-Small Cell Lung Cancer Whose Tumors Have Epidermal Growth Factor Receptor (EGFR) Exon 19 Deletions or Exon 21(L858R) Substitution Mutations	4	Maryland, Illinois
AZD9291, Erlotinib, Gefitinib	NCT02296125	To assess the efficacy and safety of AZD9291 versus a standard of care epidermal growth factor receptor tyrosine kinase inhibitor in patients with locally advanced or Metastatic Non Small Cell Lung Cancer	3	New Jersey, New York
Rociletinib, Pemetrexed, gemcitabine, paclitaxel, docetaxel	NCT02322281	TIGER-3: A Phase 3, Open-label, Multicenter, Randomized Study of Oral Rociletinib (CO-1686) Monotherapy Versus Single-agent Cytotoxic Chemotherapy in Patients With Mutant EGFR Non-small Cell Lung Cancer (NSCLC) After Failure of at Least 1 Previous EGFR-directed Tyrosine Kinase Inhibitor (TKI) and Platinum-doublet Chemotherapy	3	New Jersey, Virginia
Ramucirumab, Erlotinib	NCT02411448	A Multicenter, Randomized, Double-Blind Study of Erlotinib in Combination With Ramucirumab or Placebo in Previously Untreated Patients With EGFR Mutation-Positive Metastatic Non-Small Cell Lung Cancer	3	New York, Massachusetts
Afatinib Dimaleate, Cetuximab	NCT02438722	A Randomized Phase II/III Trial of Afatinib Plus Cetuximab Versus Afatinib Alone in Treatment-Naive Patients With Advanced, EGFR Mutation Positive Non-small Cell Lung Cancer (NSCLC)	2, 3	New Jersey, Pennsylvania
Afatinib, AZD9291	NCT02465060	EAY131: Molecular Analysis for Therapy Choice (NCI-MATCH)	2	New Jersey, New York
Rociletinib, Erlotinib	NCT02186301	TIGER 1: A Randomized, Open-Label, Phase 2 Study of CO-1686 or Erlotinib as First-Line Treatment of Patients With EGFR-Mutant Advanced NSCLC	2	New Jersey, New York

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EGFR Associated Clinical Trials				
Therapies	**NCT ID**	**Title**	**Phase**	**Locations#**
Afatinib	NCT01746251	Randomized Phase II Study Comparing Concise Versus Prolonged Afatinib as Adjuvant Therapy for Patients With Resected Stage I-III NSCLC With EGFR Mutation	2	New York, Massachusetts
Erlotinib, Bevacizumab	NCT01532089	A Randomized Phase II Trial of Erlotinib Alone or In Combination With Bevacizumab in Patients With Non-Small Cell Lung Cancer and Activating Epidermal Growth Factor Receptor Mutations	2	New York, New Hampshire
Ficlatuzumab, Erlotinib	NCT02318368	A Phase 2, Multicenter, Randomized, Double-blind Study of Ficlatuzumab Plus Erlotinib Versus Placebo Plus Erlotinib in Subjects Who Have Previously Untreated Metastatic, EGFR-mutated Non-small Cell Lung Cancer (NSCLC) and BDX004 Positive Label	2	New York, Ohio
PF-06747775	NCT02349633	Phase 1/2 Open-Label Study Of PF-06747775 (Epidermal Growth Factor Receptor T790M Inhibitor) In Patients With Advanced Epidermal Growth Factor Receptor (EGFR) Mutant (Del 19 Or L858R +/- T790M) Advanced Non-Small Cell Lung Cancer	1, 2	Connecticut, Pennsylvania
BKM120 and Erlotinib	NCT01487265	Phase II Trial of Erlotinib and BKM120 in Patients With Advanced Non Small Cell Lung Cancer Previously Sensitive to Erlotinib	2	Ohio, Florida

 # The two locations closest to the patient's address based on zip code are shown.

Please note: Select clinical trials are shown. For a full list of clinical trials, please search the ClinicalTrials.gov website.

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About Mutations

EGFR

Epidermal growth factor receptor (EGFR) belongs to a family of receptor tyrosine kinases (RTKs) that include EGFR/ERBB1, HER2/ERBB2/NEU, HER3/ERBB3, and HER4/ERBB4. The binding of ligands, such as epidermal growth factor (EGF), induces a conformational change that facilitates receptor homo- or heterodimer formation, thereby resulting in activation of EGFR tyrosine kinase activity. Activated EGFR then phosphorylates its substrates, resulting in activation of multiple downstream pathways within the cell, including the PI3K-AKT-mTOR pathway, which is involved in cell survival, and the RAS-RAF-MEK-ERK pathway, which is involved in cell proliferation.

Mutation location in gene and/or protein
Kinase domain (exon 19)

Mutation prevalence
Frequency of *EGFR* mutations in NSCLC: ~10%
Frequency of Exon19 deletions in *EGFR*-mutated NSCLC: 48%

Effect of mutation
Increase the kinase activity of EGFR, leading to hyperactivation of downstream pro-survival signaling pathways

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Cancer Drug Information

IRESSA® (gefitinib, ZD1839)
http://www.accessdata.fda.gov/drugsatfda_docs/label/2005/021399s008lbl.pdf

TARCEVA® (erlotinib)
http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/021743s018lbl.pdf

GILOTRIF® (afatinib)
http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/201292s002lbl.pdf

ABRAXANE® (Paclitaxel)
http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/021660s041lbl.pdf

PACLITAXEL INJECTION (Paclitaxel)
http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/020262s051lbl.pdf

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Table 1: OncoGxLung™ Panel Genes

OncoGxLung™ is an amplicon-based cancer test panel designed to provide sensitive and accurate genomic analysis on genes frequently mutated in cancers, EGFR, KRAS, BRAF, ALK and ROS1. Using Next Generation Sequencing (NGS) based technology, this test detects point mutations, small insertions/deletions for EGFR, KRAS and BRAF and detects selected gene fusions for ALK and ROS1 listed in the table below.

HGNC gene name	RefSeq Accession	Detectable Exons
BRAF	NP_004324	e11, e15
EGFR	NP_005219	e18, e19, e20, e21
KRAS	NP_004976	e2, e3
HGNC gene name	**RefSeq Accession**	**Detectable fusion partner genes**
ROS1	NP_002935	CD74, SLC34A2, GOPC, EZR, SDC4, TPM3, LRIG3
ALK	NP_004295	KIF5B, TFG, EML4

References:

- NCCN Biomarkers Compendium at: http://www.nccn.org/professionals/biomarkers/content/
- U.S. Food and Drug Administration, Table of Pharmacogenomic Biomarkers in Drug Labeling. Available online at: http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm083378.htm
- My Cancer Genome at: http://www.mycancergenome.org/
- PharmGKB: The Pharmacogenomics Knowledgebase. Available online at: http://www.pharmgkb.org/index.jsp
- The Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline. Available online at: https://www.pharmgkb.org/page/cpic
- European Medicines Agency, Multidisciplinary: Pharmacogenomics. Available online at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000411.jsp&mid=WC0b01ac058002958e
- Swen JJ et al. Pharmacogenetics: from bench to byte - an update of guidelines. Clin Pharmacol Ther. 2011 May;89(5):662-73.
- Ramalingam SS et al. Randomized phase II study of dacomitinib (PF-00299804), an irreversible pan-human epidermal growth factor receptor inhibitor, versus erlotinib in patients with advanced non-small-cell lung cancer. J Clin Oncol. 2012 Sep 20;30(27):3337-44.
- Jänne PA et al. AZD9291 in EGFR Inhibitor-Resistant Non-Small-Cell Lung Cancer. 2015 Apr 30;372(18):1689-99.
- Hertz DL et al. CYP2C8*3 increases risk of neuropathy in breast cancer patients treated with paclitaxel. Ann Oncol. 2013 Jun;24(6):1472-8.

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Test Methodology and Limitations for OncoGxLung™:

Target regions of interest were constructed using an amplicon library and sequenced by massive parallel sequencing method (Illumina platform). The detected mutations are annotated based on hG19 reference genome assembly. The OncoGxLung™ test was developed by Admera Health, including determination and validation of performance characteristics. The sensitivity and specificity of this test is greater than 99.9% and 99.9%, respectively, when a minimum of 10% tumor tissue is present in the sample. This test has not been approved by the U.S. Food and Drug Administration (FDA) but the FDA has determined that such clearance or approval is not necessary. The OncoGxLung™ test is used for clinical purposes. It should not be regarded as investigational or for research. The Admera Health clinical laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), accredited by the College of American Pathologists, and is qualified to perform high complexity clinical laboratory testing.

Disclaimer of Liability:

The information contained in this report is provided as a service and does not constitute medical advice. At the time of report generation this information is believed to be current and is based upon published research; however, research data evolves and amendments to the prescribing information of the drugs listed will change over time. While this report is believed to be accurate and complete as of the date issued, THE DATA IS PROVIDED "AS IS", WITHOUT WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION, THE IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE. As medical advice must be tailored to the specific circumstances of each case, the treating health care professional has ultimate responsibility for all treatment decisions made with regard to a patient including any made on the basis of a patient's genotype.

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