GeneStrat® Report

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Patient: <**PtFirst and LastName**>
DOB: <Mon DD, YYYY>
Gender: <Gender>
Tumor: <Type>
Specimen Type: Peripheral Whole Blood

GS Accession No: BDXA########-xxx
Date of Collection: <Mon DD, YYYY>
Date Received: <Mon DD, YYYY>
Date Performed/Reported: <Mon DD, YYYY>

Physician: Dr. <PhysFirst and LastName>
Facility: <Ordering Facility Name>
Address: <Street Address>
Address: <City, State Postal Code>
Country: <Country Code>
Phone: <Phone Number>
Fax: <Fax Number>

genestrat® genomic test

Test	Variant	Results
EGFR Mutations	Exon 19 Δ E746-A750	**POSITIVE**
	Exon 21 L858R	Negative
	Exon 20 T790M	Negative
ALK Fusions	EML4	Negative
ROS1 Fusions	CD74, SDC4, SLC34A2, EZR, TPM3	Negative
RET Fusions	KIF5B, CCDC6, TRIM33	Negative
KRAS Mutations	G12C	Negative
	G12D	Negative
	G12V	Negative
BRAF Mutation	V600E	Negative

Interpretation of Results

EGFR, ALK, ROS1*, RET*, KRAS, BRAF
Positive: Presence of 2 or more copies of the variant
Negative: Presence of less than 2 copies of the variant
QNS: Test performed, and results not definitive - due to lack of sufficient amount of nucleic acid.
No bill will be submitted for this gene. Redraw recommended.
*For a Positive Result, presence of 10 or more copies of the variant
*For a Negative Result, presence of less than 10 copies of the variant

Definitions
TNP: Test Not Performed
QNS: Quantity Not Sufficient

Donald Joe Chaffin, M.D., CAP Accredited CLIA Laboratory Director

GeneStrat® Treatment Implications

Available Mutations	Treatment Implications for Non-small Cell Lung Cancer[8-20]
EGFR Sensitizing Exon 19 ΔE746-A750 Exon 21 L858R	May benefit from treatment with afatinib, erlotinib, gefitinib, or osimertinib
EGFR Resistance Exon 20 T790M	May benefit from treatment with osimertinib if previously treated with 1st or 2nd generation EGFR-TKIs
ALK EML4	May benefit from treatment with crizotinib, ceritinib, alectinib or brigatinib depending on previous therapies
ROS1 CD74, SDC4, SLC34A2, EZR, TPM3	May benefit from treatment with crizotinib
RET KIF5B, CCDC6, TRIM33	May benefit from treatment with cabozantinib
KRAS G12C, G12D, G12V	KRAS mutations are associated with poorer prognosis
BRAF V600E	May benefit from dabrafenib + trametinib, vemurafenib, or dabrafenib

GeneStrat® Analysis Description: GeneStrat® genomic testing is a laboratory test service that determines the presence of somatic genetic variants in circulating nucleic acids (DNA and RNA) from the plasma of patients with cancer using ddPCR (droplet digital polymerase chain reaction)[1-2]. In the ddPCR process, a patient sample is dispersed in an emulsion so that individual nucleic acid molecules are isolated. After amplification, nucleic acids are quantified by counting the emulsion that contains PCR end-product, or positive reactions[4]. GeneStrat is a genomic approach to detection of insertion, deletions and point mutations[1], as well as fusion products[2,3,4,6].

GeneStrat solely reports the presence or absence of certain, limited genomic alterations which may be useful for physicians when considering different therapeutic options. The mutations detected using the GeneStrat test account for a large proportion of variants found in NSCLC, including EGFR (84% coverage)[21], ALK (78%)[4], ROS1 (88%)[21], RET (99%)[21], KRAS (78%)[21], and BRAF (54%)[21]. Accordingly, results are adjunctive to the ordering physician's workup and should be evaluated by a qualified healthcare professional in combination with the patient's clinical history, other diagnostic tests, and clinicopathological factors. For patients that test negative for all mutations, tissue biopsy can be considered. Any questions regarding the use of the GeneStrat test or interpretation of the test results should be directed to Biodesix Customer Support at 866-432-5930.

References:

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3. Mellert, et al. A Blood-based Test for the Detection of ROS1 and RET Fusion Transcripts from Circulating Ribonucleic Acid using Digital Polymerase Chain Reaction. JoVE 2017. (in Press).
4. Maus et.al. Identification of Novel Variant of EML4-ALK Fusion Gene in NSCLC: Potential Benefits of the RT-PCR Method. Maus MK, Stephens C, Zeger G, Grimminger PP, Huang E. Int J Biomed Sci. 2012 Mar;8(1):1-6.
5. Oxnard GR et al. Noninvasive detection of response and resistance in EGFR-mutant lung cancer using quantitative next-generation genotyping of cell-free plasma DNA. Clin Cancer Res. 2014;20(6):1698-1705.
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7. Gilotrif (afatinib), Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA.
8. Tarceva (erlotinib), Astellas Oncology Inc., Northbrook, IL, USA.
9. Iressa (gefitinib), AstraZeneca Pharmaceuticals, LP, Wilmington, DE, USA.
10. Tagrisso (osmertinib), AstraZeneca Pharmaceuticals, LP, Wilmington, DE, USA.
11. Xalkori (crizotinib), Pfizer Inc., New York, NY, USA.
12. Zykadia (ceritinib), Novartis Pharmaceuticals Corporation East Hanover, NJ, USA.
13. Alecensa (alectinib), Genentech, Inc. A Member of the Roche Group, South San Francisco, CA, USA.
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16. Hyman DM, Puzanov I, et al. Vemurafenib in multiple nonmelanoma cancers with BRAF (V600E). N Engl J Med 2015; 373:726-736.
17. Gautschi O, et al. Target Therapy for Patients with BRAF-Mutant Lung Cancer: Results from the European EURAF cohort. J Thorac Oncol 2015;10:1451-1457.
18. Planchard D, et al. Dabrafenib in patients with BRAF (V600E)-positive advanced non-small cell lung cancer: an open-label, multicentre phase 2 trial. Lancet Oncol 2016;17:642-650.
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20. Alunbrig (brigatinib), Takeda Oncology, Cambridge, MA, USA.
21. COSMIC database: v79, released 14-NOV-2016. http://cancer.sanger.ac.uk/cosmic

GeneStrat was developed and its performance characteristics were determined by Biodesix, Inc. The Biodesix laboratory meets the requirements for high complexity tests under the Clinical Laboratory Improvement Amendments of 1988, as amended, and its implementing regulations.

By accepting receipt of the GeneStrat Test Result Report or any content derived from it ("GS TRR"), the ordering physician, institution of ordering Physician, or any third parties to whom the GS TRR is transferred, agree the GS TRR may only be used for the clinical management of the patient identified in the GS TRR by the ordering physician. Any other use of the GS TRR including, without limitation, correlative studies, diagnostic development, derivative works or other analyses, is expressly prohibited. The results of any unauthorized use of the GS TRR shall belong solely and exclusively to Biodesix, Inc. Additional terms and conditions related to this GS TRR can be found at www.biodesix.com.