genestrat® genomic test

Phone: **1.866.432.5930** | Fax: **1.866.432.3338**
Email: **custcare@biodesix.com**

Test Result Report

PATIENT INFORMATION		PHYSICIAN INFORMATION	
Patient: <First and LastName>		**Physician:** Dr. <First and LastName>	
Date of Birth: <Mon DD, YYYY>	**Gender:** <Gender>	**Facility:** <Ordering Facility Name>	
Tumor: <Tumor Type>	**Specimen Type:** <Sample Format>	**Address:** <Street Address, City, State, Postal Code>	
GS Accession No: BDXA########-XXX	**Date of Collection:** <Mon DD, YYYY>	**Country:** <Country Code>	
Date Received: <Mon DD, YYYY>	**Date Performed | Reported:** <Mon DD, YYYY>	**Phone:** <Phone Number>	**Fax:** <Fax Number>

GENESTRAT® GENOMIC TEST RESULTS

Test	Variant	Results
EGFR Sensitizing	Exon 19 ΔE746-A750	**POSITIVE**
	Exon 21 L858R	Negative
	Exon 18 G719A, G719C, G719S | Exon 20 S768I | Exon 21 L861Q	Negative
EGFR Resistance	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 fewer 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 fewer than 10 copies of the variant

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

biodesix.com
2970 Wilderness Place, Suite 100, Boulder, CO 80301

biodesix®

genestrat® genomic test

Phone: **1.866.432.5930** | Fax: **1.866.432.3338**
Email: **custcare@biodesix.com**

GENESTRAT® TREATMENT IMPLICATIONS

Available Mutations	Treatment Implications for Non-Small Cell Lung Cancer[1-14]
EGFR Sensitizing Exon 19 ΔE746-A750 | Exon 21 L858R	May benefit from treatment with osimertinib, afatinib, erlotinib, gefitinib or dacomitinib
Exon 18 G719A, G719C, G719S | Exon 20 S768I | Exon 21 L861Q	May benefit from treatment with afatinib
EGFR Resistance Exon 20 T790M	May benefit from treatment with osimertinib if previously treated with 1st or 2nd generation EGFR-TKIs
ALK Fusions EML4	May benefit from treatment with alectinib, brigatinib, ceritinib, crizotinib or lorlatinib
ROS1 Fusions CD74 | SDC4 | SLC34A2 | EZR | TPM3	May benefit from treatment with crizotinib, ceritinib or lorlatinib
RET Fusions KIF5B | CCDC6 | TRIM33	May benefit from treatment with cabozantinib or vandetinib
KRAS Mutations G12C | G12D | G12V	KRAS mutations are associated with poorer prognosis
BRAF Mutation 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 lung cancer using ddPCR (Droplet Digital™ Polymerase Chain Reaction)[15,16]. 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[17]. GeneStrat is a genomic approach to detection of insertion, deletions and point mutations[15], as well as fusion products[16,17,18,19,20].

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 GeneStrat account for a large proportion of variants found in NSCLC, including EGFR (89% coverage)[21], ALK (78%)[17], ROS1 (88%)[22], RET (99%)[22], KRAS (78%)[22], and BRAF (54%)[22]. 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 Care at 1.866.432.5930.

REFERENCES:

1. Tagrisso (osimertinib), AstraZeneca Pharmaceuticals, LP, Wilmington, DE, USA.
2. Gilotrif (afatinib), Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA.
3. Tarceva (erlotinib), Astellas Oncology Inc., Northbrook, IL, USA.
4. Iressa (gefitinib), AstraZeneca Pharmaceuticals, LP, Wilmington, DE, USA.
5. Vizimpro (dacomitinib), Pfizer Inc., New York, NY, USA.
6. Alecensa (alectinib), Genentech, Inc. A Member of the Roche Group, South San Francisco, CA, USA.
7. Alunbrig (brigatinib), Takeda Oncology, Cambridge, MA, USA.
8. Zykadia (ceritinib), Novartis Pharmaceuticals Corporation East Hanover, NJ, USA.
9. Xalkori (crizotinib), Pfizer Inc., New York, NY, USA.
10. Lorbrena (lorlatinib), Pfizer Inc., New York, NY, USA.
11. Drilon A, et al. Response to cabozantinib in patients with RET fusion-positive lung adenocarcinomas. Cancer Discov 2013; 3:630-635.
12. Drilon A, et al. Cabozantinib in patients with RET-rearranged NSCLC: an open-label, single-centre, phase 2, single-arm trial. Lancet Oncol 2016; 17:1653-1660.
13. Lee SH, et al. Vandetinib in pretreated patients with advanced NSCLC-harboring RET rearrangement: a phase II clinical trial. Ann Oncol 2017; 28:292-297.
14. Tafinlar + Mekinist (Dabrafenib + Mekinist), Novartis Pharmaceuticals Corporation East Hanover, NJ, USA.
15. Vogelstein B, Kinzler KW. Digital PCR. PNAS.1999;96(16):9236-9241.
16. Mellert H, Foreman T, Jackson L, Maar D, Thurston S, Koch K, Weaver A, Cooper S, Dupuis N, Sathyanarayana UG, Greer J, Hahn W, Shelton D, Stonemetz P, Pestano GA: Development and Clinical Utility of a Blood-based Test Service for the Rapid Identification of Actionable Mutations in NSCLC Journal of Molecular Diagnostics 2017.
17. 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.
18. 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. J. Vis. Exp. (134), e57079, doi:10.3791/57079 (2018).
19. 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.
20. Wang Y et al. EML4-ALK fusion detected by RT-PCR confers similar response to crizotinib as detected by FISH in patients with advanced NSCLC. J Thorac Oncol. 2015;10(11):1546-1552.
21. Kobayashi Y, Mitsudomi T. Not all epidermal growth factor receptor mutations in lung cancer are created equal: Perspectives for individualized treatment strategy. Cancer Sci. 2016;107(9):1179–1186. doi:10.1111/cas.12996.
22. 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.

Patient:
<First and LastName>

GS Accession No:
BDXA########-XXX

Date Performed | Reported:
<Mon DD, YYYY>

biodesix®