genestrat NGS genomic test

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RESULTS REPORT

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PATIENT	PHYSICIAN	SPECIMEN	CASE
PATIENT Jane Smith **MRN #** 000-000-001 **DISEASE#** Malignant tumor of lung, Advanced stage (IIIB/IV) **DATE OF BIRTH** 11/23/1988 **SEX** Female	**ORDERING PHYSICIAN** Dr. John Doe **FACILITY** Biodesix **ADDRESS** Street City, ST Zip **FAX** (###) ###-####	**SPECIMEN TYPE** Peripheral Whole Blood **EXT. SPECIMEN ID** 48998243 **DATE COLLECTED** 11/02/2019 **DATE RECEIVED** 11/06/2019	**REVIEW STATUS** Final **DATE REPORTED** 11/10/2021 **ACCESSION #** BDX_447

An EGFR p.L858R mutation was detected in this sample. This mutation is considered an activating mutation in lung cancer, and may indicate response to EGFR tyrosine kinase inhibitor therapy.

I A	I B	II C	II D	Trials
1	0	1	0	4

RELEVANT THERAPIES

Tier	Variant Detected (Gene/Syntax)	Clinical Impact		Select Clinical Trials
IA	EGFR p.L858R	**May benefit from:**	Icotinib, Afatinib + Cetuximab, Erlotinib, Afatinib, Bevacizumab+ Erlotinib, Erlotinib + Ramucirumab, Dacomitinib, Osimertinib, or Gefitinib	2
		In Tumor Type:	Malignant tumor of lung	
II C	TP53 p.R273H	**Not likely to benefit from:**	Cyclophosphamide, Fludarabine, or Rituximab	2
		In Tumor Type:	Chronic lymphoid leukemia	
		Unfavorable Prognosis in:	Medulloblastoma, Acute myeloid leukemia, or Myelodysplastic syndrome	

Report electronically reviewed and signed out by: Benjamin Pierce, MD
Date Reported: 11/10/2021

CLINICAL TRIALS

Clinical Trials associated with this patient's genomic profile and tumor type are displayed below.

Title	Trial Identifier	Phase	Variant
Phase 2 Study of Poziotinib in Patients With NSCLC Having EGFR or HER2 Exon 20 Insertion Mutation	NCT03318939	II	**EGFR** p.L858R
Study of Osimertinib With and Without Ramucirumab in Locally Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC)	NCT03909334	II	**EGFR** p.L858R
Phase 1/2 Study of APR-246 in Combination With Pembrolizumab in Subjects With Solid Tumor Malignancies	NCT04383938	I/II	**TP53** p.R273H
Study of AMG 650 in Adult Participants With Advanced Solid Tumors	NCT04293094	I	**TP53** p.R273H

COMPREHENSIVE CLINICAL INTERPRETATIONS

EGFR	**p.L858R**	c.2573T>G	Tier 1	NM_005228.3	VAF 7.6%	Depth 858

EGFR encodes a receptor tyrosine kinase activated by members of the epidermal growth factor family and is involved in cell proliferation, metastasis, migration and prevention of apoptosis (PMID: 27843613, 2016). Afatinib in combination with cetuximab is NCCN (Non-Small Cell Lung Cancer, 7.2019) guideline recommended for use in non-small cell lung cancer harboring a sensitizing EGFR mutation, as subsequent therapy following disease progression on EGFR tyrosine kinase inhibitor therapy. Atezolizumab in combination with bevacizumab and chemotherapeutic agents is ESMO (PMID: 30285222, 2018; https://www.esmo.org/Guidelines/Lung-and-Chest- Tumours/Metastatic-Non-Small-Cell-Lung-Cancer, 2019) guideline recommended for use in metastatic nonsquamous non-small cell lung cancer harboring a sensitizing EGFR mutation, in the absence of contraindications to the use of immunotherapy after targeted therapies have been exploited. Bevacizumab in combination with erlotinib is EMA (Bevacizumab Avastin, Revision 52; Bevacizumab Mvasi, Revision 5)approved for use in adult nonsquamous non-small cell lung cancer harboring an activating EGFR mutation, as a first-line therapy. Per the EMA, the safety and efficacy of bevacizumab in combination with erlotinib in the pediatric population has not been established. Bevacizumab in combination with erlotinib is ESMO (PMID: 30285222, 2018; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer, 2019) guideline recommended for use in non-small cell lung cancer harboring an EGFR mutation, as a first-line therapy. Erlotinib in combination with ramucirumab is ESMO (PMID: 30285222, 2018; https://www.esmo.org/Guidelines/ Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer, 2019) guideline recommended for use in non-small cell lung cancer harboring an EGFR mutation, as a first-line therapy. Afatinib is FDA (Afatinib, 201292s015lbl) and EMA (Afatinib, Revision 11) approved and NCCN (Non-Small Cell Lung Cancer, 7.2019), ASCO (PMID: 28806116, 2017) and ESMO (PMID: 30285222, 2018; https://www.esmo.org/ Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer, 2019) guideline recommended as a monotherapy for use in non-small cell lung cancer harboring a sensitizing EGFR mutation, as a first-line therapy or for continuation on disease progression.

TP53	**p.R273H**	c.818G>A	Tier IIC	NM_001126114.2	VAF 6.9%	Depth 721

TP53 is a tumor suppressor and regulates expression of target genes by inducing cell cycle arrest, apoptosis, senescence, DNA repair, or changes in metabolism (PMID:22294769, 2012; PMID: 20182602, 2010). Some evidence indicates that recurrent adenocarcinoma of lung harboring an ERBB2 p.(Tyr772_Ala775dup) mutation co occurring with a TP53 p.(Arg273His) mutation may not benefit from afatinib based on progression-free survival in a multi center retrospective study of 32 participants (PMID:31748336, 2019).

TEST INFORMATION

TEST DESCRIPTION: The GeneStrat NGS™ genomic test is a qualitative laboratory developed test designed to aid physicians by providing molecular characterization of cancer patients' disease. The test has been validated for the detection of somatic mutations from cell-free nucleic acids (cfDNA) derived from plasma samples using established targeted next generation sequencing methodology.

GENES ASSAYED: *AKT1, ALK, AR, ARAF, BRAF, CHEK2, CTNNB1, DDR2, EGFR, ERBB2, ERBB3, ESR1, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, GNA11, GNAQ, GNAS, HRAS, IDH1, IDH2, KIT, KRAS, MAP2K1, MAP2K2, MET, MTOR, NRAS, NTRK1, NTRK3, PDGFRA, PIK3CA, RAF1, RET, ROS1, SF3B1, SMAD4, SMO, APC, FBXW7, PTEN, TP53*

LIMITATIONS AND DISCLAIMER:

- Specific validated SNV and indel variant types relevant to oncology are reported from the genes assayed.
- The test has been validated to 0.5% Variant Allele Frequency for SNVs and indels.
- The limit of detection for fusion/skipping variants and copy number variants (CNVs) were 42 copies and 1.4 fold change, respectively.
- Reported variants may be either somatic (not inherited) or germline (inherited). The GeneStrat NGS™ genomic test cannot discern the source of the cfDNA, and for some variants in the range of ~40 to 60% minor allele frequency, the test cannot easily distinguish germline variants from somatic alterations. If a reported alteration is suspected to be germline, confirmatory testing should be considered in the appropriate clinical context.
- Variants found in circulation may be due to clonal hematopoiesis of indeterminate potential (CHIP). 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 variants, tissue biopsy is recommended.
- The GeneStrat NGS™ genomic test was developed and its performance characteristics determined by Biodesix, Inc. as a laboratory developed test. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA does not require this test to go through premarket FDA review. This test is used for clinical purposes and should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high-complexity clinical laboratory testing.
- The GeneStrat NGS™ genomic test results are intended to assist with decisions related to patient management and provide supplementary information. This test is not a stand-alone diagnostic assay.