FoundationOne®CDx

Patient Guide: Understanding the Report with Your Doctor

This FoundationOne® CDx report guide will help you understand each section of your report. Use this guide after your results are ready. Once you review the results with your doctor, together you can decide the next best step in your treatment plan.

Definitions of key terms are on the last page of this guide.

report page one

1 Genomic Findings Detected

If mutations are found in your tumor sample, these mutations will be listed as "genomic findings detected" in your report. This section includes the name of the gene (e.g., "*ALK*") along with the description of the mutation within that gene (e.g., "*EML4-ALK* fusion").

2 FDA-Approved Therapeutic Options

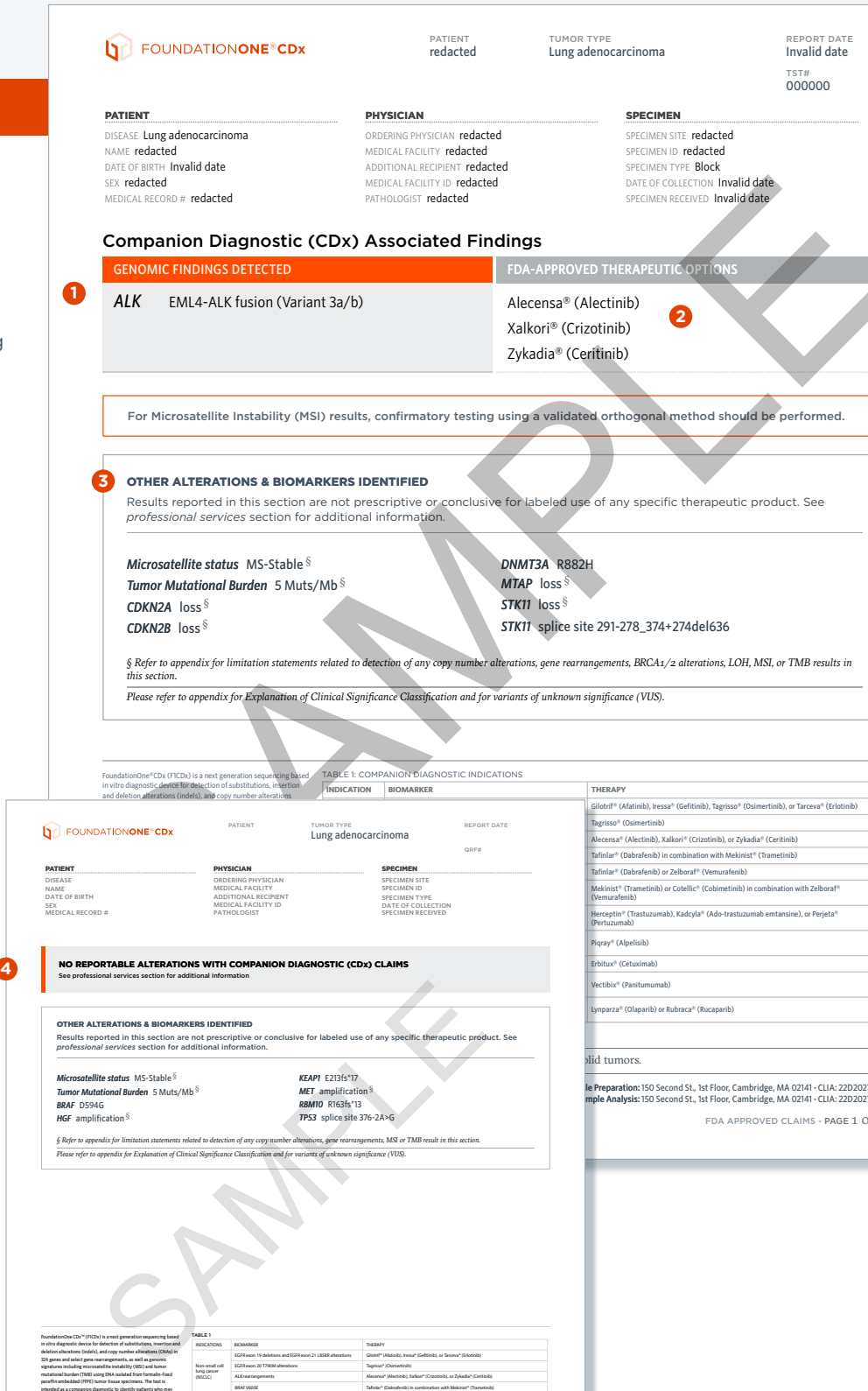
The test is an FDA-approved "companion diagnostic" (or "CDx") for certain treatments. This means that the FDA has extensively reviewed and approved the test to be used to identify patients who may benefit from these treatments. This section lists treatment options linked with specific gene mutations found in your tumor. Your doctor will determine if any of these treatments may be right for you.

3 Other Alterations & Biomarkers Identified

A list of additional genomic findings in the report are listed in this section. These findings, along with associated targeted therapies, are described in the following pages of the report.

4 No Reportable Alterations with CDx Claims

It is possible that there are no treatment options listed in this CDx section—this is not uncommon and there may be other options on the following pages of your report. Talk to your doctor about the treatment options in your full report.



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PATIENT redacted | TUMOR TYPE Lung adenocarcinoma | REPORT DATE Invalid date | TST# 000000

PATIENT
DISEASE Lung adenocarcinoma
NAME redacted
DATE OF BIRTH Invalid date
SEX redacted
MEDICAL RECORD # redacted

PHYSICIAN
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PATHOLOGIST redacted

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Companion Diagnostic (CDx) Associated Findings

1 GENOMIC FINDINGS DETECTED	FDA-APPROVED THERAPEUTIC OPTIONS
ALK EML4-ALK fusion (Variant 3a/b)	Alecensa® (Alectinib) Xalkori® (Crizotinib) Zykadia® (Ceritinib) 2

For Microsatellite Instability (MSI) results, confirmatory testing using a validated orthogonal method should be performed.

3 OTHER ALTERATIONS & BIOMARKERS IDENTIFIED

Results reported in this section are not prescriptive or conclusive for labeled use of any specific therapeutic product. See *professional services* section for additional information.

Microsatellite status MS-Stable §
Tumor Mutational Burden 5 Muts/Mb §
CDKN2A loss §
CDKN2B loss §
DNMT3A R882H
MTAP loss §
STK11 loss §
STK11 splice site 291-278_374+274del636

§ Refer to appendix for limitation statements related to detection of any copy number alterations, gene rearrangements, BRCA1/2 alterations, LOH, MSI, or TMB results in this section.

Please refer to appendix for Explanation of Clinical Significance Classification and for variants of unknown significance (VUS).

FoundationOne®CDx (F1CDx) is a next generation sequencing based in vitro diagnostic device for detection of substitutions, insertion and deletion alterations (indels), and copy number alterations

TABLE 1: COMPANION DIAGNOSTIC INDICATIONS

INDICATION	BIOMARKER	THERAPY
Non-small cell lung cancer (NSCLC)	EGFR exon 19 deletions and EGFR exon 21 L858R alterations	Gilotrif® (Afatinib), Iressa® (Gefitinib), Tagrisso® (Osimertinib), or Tarceva® (Erlotinib)
	EGFR exon 20 T790M alterations	Tagrisso® (Osimertinib)
	ALK rearrangements	Alecensa® (Alectinib), Xalkori® (Crizotinib), or Zykadia® (Ceritinib)
	BRAF V600E	Tafinlar® (Dabrafenib) in combination with Mekinist® (Trametinib)
		Tafinlar® (Dabrafenib) or Zelboraf® (Vemurafenib)
		Mekinist® (Trametinib) or Cotellic® (Cobimetinib) in combination with Zelboraf® (Vemurafenib)
	HER2 amplification	Herceptin® (Trastuzumab), Kadcyla® (Ado-trastuzumab emtansine), or Perjeta® (Pertuzumab)
	PIK3CA mutations	Piqray® (Alpelisib)
	EGFR exon 18 G719A, exon 21 L861Q, and exon 20 S768I alterations	Erbitux® (Cetuximab)
	KRAS exon 2 G12D alterations	Vectibix® (Panitumumab)
Ovarian cancer	BRCA1/2 alterations	Lynparza® (Olaparib) or Rubraca® (Rucaparib)

olid tumors.

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PATIENT | TUMOR TYPE Lung adenocarcinoma | REPORT DATE | QRF#

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4 **NO REPORTABLE ALTERATIONS WITH COMPANION DIAGNOSTIC (CDx) CLAIMS**
See professional services section for additional information

OTHER ALTERATIONS & BIOMARKERS IDENTIFIED

Results reported in this section are not prescriptive or conclusive for labeled use of any specific therapeutic product. See *professional services* section for additional information.

Microsatellite status MS-Stable §
Tumor Mutational Burden 5 Muts/Mb §
BRAF D594G
HGF amplification §
KEAP1 E213fs*17
MET amplification §
RBM10 R163fs*13
TP53 splice site 376-2A>G

§ Refer to appendix for limitation statements related to detection of any copy number alterations, gene rearrangements, MSI or TMB result in this section.

Please refer to appendix for Explanation of Clinical Significance Classification and for variants of unknown significance (VUS).

FoundationOne CDx™ (F1CDx) is a next generation sequencing based in vitro diagnostic device for detection of substitutions, insertion and deletion alterations (indels), and copy number alterations (CNAs) in 324 genes and select gene rearrangements, as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB) using DNA isolated from formalin-fixed paraffin-embedded (FFPE) tumor tissue specimens. The test is intended as a companion diagnostic to identify patients who may

TABLE 1

INDICATIONS	BIOMARKER	THERAPY
Non-small cell lung cancer (NSCLC)	EGFR exon 19 deletions and EGFR exon 21 L858R alterations	Gilotrif® (Afatinib), Iressa® (Gefitinib), or Tarceva® (Erlotinib)
	EGFR exon 20 T790M alterations	Tagrisso® (Osimertinib)
	ALK rearrangements	Alecensa® (Alectinib), Xalkori® (Crizotinib), or Zykadia® (Ceritinib)
	BRAF V600E	Tafinlar® (Dabrafenib) in combination with Mekinist® (Trametinib)

Page two of your report contains additional biomarker and genomic findings and associated therapies that may be options for your doctor to consider for your treatment plan.

report page two

5

Biomarker Findings

This section refers to two biomarkers that may be linked to immunotherapy treatment options—microsatellite instability (MSI) and tumor mutational burden (TMB). Your doctor may use these biomarkers to determine if immunotherapy could be right for you.

6

Genomic Findings

This section shows the gene mutations found in your tumor DNA that may be linked with targeted therapy options.

It is possible that your test did not find mutations in genes commonly mutated in your cancer type. Based on this information your doctor may avoid certain treatments or determine an alternate course of care.

7

Therapies with Clinical Benefit

These are potential treatment options that may be relevant for you based on your gene mutations. The type of treatments in this section may be targeted therapies or immunotherapies.

The therapies listed in the middle column are FDA-approved for your cancer type. The therapies in the right column are FDA-approved for another cancer type. Your doctor will determine if any of these treatments may be right for you.

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PATIENT redacted

TUMOR TYPE Lung adenocarcinoma
COUNTRY CODE redacted

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ABOUT THE TEST FoundationOne®CDx is the first and only FDA-Approved comprehensive companion diagnostic for all solid tumors.

Interpretive content on this page and subsequent pages is provided as a professional service, and is not reviewed or approved by the FDA.

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Biomarker Findings 5
Microsatellite status - MS-Stable
Tumor Mutational Burden - 5 Muts/Mb

Genomic Findings 6
For a complete list of the genes assayed, please refer to the Appendix.
ALK EML4-ALK fusion (Variant 3a/b)
STK11 splice site 291-278_374+274del636, loss exon 2
CDKN2A/B loss
DNMT3A R882H
MTAP loss

7 Disease relevant genes with no reportable alterations: ***EGFR, KRAS, BRAF, MET, RET, ERBB2, ROS1***

8 Therapies with Clinical Benefit
0 Therapies with Lack of Response
19 Clinical Trials

BIOMARKER FINDINGS	ACTIONABILITY
Microsatellite status - MS-Stable	**No therapies or clinical trials.** see Biomarker Findings section
Tumor Mutational Burden - 5 Muts/Mb	**No therapies or clinical trials.** see Biomarker Findings section

GENOMIC FINDINGS	THERAPIES WITH CLINICAL BENEFIT (IN PATIENT'S TUMOR TYPE)		THERAPIES WITH CLINICAL BENEFIT (IN OTHER TUMOR TYPE)
ALK - EML4-ALK fusion (Variant 3a/b)	Alectinib	1	none
	Brigatinib 7	1	
	Ceritinib	1	
	Crizotinib	1	
	Lorlatinib	2A	
	Entrectinib		
10 Trials *see p. 13*			
STK11 - splice site 291-278_374+274del636, loss exon 2	none		Everolimus
			Temsirolimus
10 Trials *see p. 16*			

NCCN category (resistance may not be reflected in NCCN category)

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PROFESSIONAL SERVICES - PAGE 1 of

Each report contains additional pages with supporting information that your doctor can use to better understand your findings and their relevance to your cancer.

the rest of the report

8

Clinical Trial Options

When applicable, your results are matched with potential treatments that are currently being tested in clinical trials. Participating in a clinical trial could help you access some of the newest treatments in development. Talk to your doctor about which clinical trials may be available and if you qualify for them.

Even if the results don't identify a specific therapy or clinical trial that may be right for you, they can still provide valuable information to you and your doctor. They may show what treatments may not be appropriate for you based on your genomic findings, they may confirm your current treatment, or point to new treatments that may become available in the future.

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8 CLINICAL TRIALS

IMPORTANT Clinical trials are ordered by gene and prioritized by: age range inclusion criteria for pediatric patients, proximity to ordering medical facility, later trial phase, and verification of trial information within the last two months. While every effort is made to ensure the accuracy of the information contained below, the information available in the public domain is continually updated and should be investigated by the physician or research staff. This is not a comprehensive list of all available clinical trials. Foundation Medicine displays a subset of trial options and ranks them in this order of descending priority: Qualification for pediatric trial → Geographical proximity → Later trial phase. Clinical trials listed here may have additional enrollment criteria that may require medical screening to determine final eligibility. For additional information about listed clinical trials or to conduct a search for additional trials, please see clinicaltrials.gov. Or, visit https://www.foundationmedicine.com/genomic-testing#support-services.

GENE *ALK*

RATIONALE ALK rearrangements, activating mutations, or amplification may predict sensitivity to ALK inhibitors as well as HSP90 inhibitors.

ALTERATION EML4-ALK fusion (Variant 3a/b)

NCT02201992 — PHASE 3

Crizotinib in Treating Patients With Stage IB-IIIA Non-small Cell Lung Cancer That Has Been Removed by Surgery and ALK Fusion Mutations (An ALCHEMIST Treatment Trial)

TARGETS ALK, AXL, MET, ROS1, TRKA, TRKC

LOCATIONS: Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, Wyoming

NCT03737994 — PHASE 2

Biomarker/ALK Inhibitor Combinations in Treating Patients With Stage IV ALK Positive Non-Small Cell Lung Cancer (The NCI-NRG ALK Master Protocol)

TARGETS ALK, RET, EGFR, ROS1, ABL, AXL, MET, TRKA, TRKC

LOCATIONS: Arizona, Arkansas, California, Colorado, Delaware, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kentucky, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Montana, Nebraska, New York, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, South Dakota, Texas, Utah, Virginia, Washington, Wisconsin, Wyoming

NCT03093116 — PHASE 1/2

A Study of TPX-0005 in Patients With Advanced Solid Tumors Harboring ALK, ROS1, or NTRK1-3 Rearrangements

TARGETS ALK, ROS1, TRKA, TRKB, TRKC

LOCATIONS: Edmonton (Canada), California, Singapore (Singapore), Colorado, District of Columbia, Florida, Georgia, Massachusetts, Michigan, Minnesota, Missouri, New Jersey, New York, Ohio, Texas, Melbourne (Australia), Washington, Seoul (Korea, Republic of), Groningen (Netherlands)

NCT02568267 — PHASE 2

Basket Study of Entrectinib (RXDX-101) for the Treatment of Patients With Solid Tumors Harboring NTRK 1/2/3 (Trk A/B/C), ROS1, or ALK Gene Rearrangements (Fusions)

TARGETS ALK, ROS1, TRKA, TRKB, TRKC

LOCATIONS: Arizona, California, Napoli (Italy), Colorado, Connecticut, District of Columbia, Florida, Georgia, Illinois, Roma (Italy), Milano (Italy), Maryland, Massachusetts, Michigan, Minnesota, Missouri, Nevada, Liverpool (Australia), New Lambton Heights (Australia), New York, North Carolina, Ohio, Oregon, Candiolo (Italy), Bedford Park (Australia), Texas, Pisa (Italy), Perugia (Italy), Utah, Padova (Italy), Heidelberg (Australia), Virginia, Washington, Edegem (Belgium), Angers (France), Bordeaux (France), Lille (France), Lyon (France), Marseille (France), Marseille cedex 5 (France), Montpellier cedex 5 (France), Paris (France), Saint Herblain (France), Toulouse (France), Villejuif cedex (France), Berlin (Germany), Dresden (Germany), Göttingen (Germany), Heidelberg (Germany), Köln (Germany), Hong Kong (Hong Kong), Kowloon (Hong Kong), Shatin (Hong Kong), Aichi (Japan), Ehime (Japan), Fukuoka (Japan), Hyogo (Japan), Kashiwa-shi (Japan), Miyagi (Japan), Niigata (Japan), Osaka (Japan), Shizuoka (Japan), Seoul (Korea, Republic of), Amsterdam (Netherlands), Leiden (Netherlands), Gdańsk (Poland), Gliwice (Poland), Poznań (Poland), Warszawa (Poland), Singapore (Singapore), Barcelona (Spain), Madrid (Spain), Malaga (Spain), Sevilla (Spain), Tainan (Taiwan), Taipei (Taiwan), Taipei City (Taiwan), Cambridge (United Kingdom), London (United Kingdom), Manchester (United Kingdom)

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Key Terms

Alterations
Changes in the DNA that can impact cancer (also referred to as "mutations").

Biomarker
A measurable characteristic within a cancer cell. The status of a biomarker may provide your doctor with information about potential treatment options.

Biomarker Findings
On your FoundationOne CDx report, the "Biomarker Findings" section refers to the genomic signatures microsatellite instability (MSI) and tumor mutational burden (TMB). A high level of either of these two biomarkers may indicate that you could benefit from immunotherapy. Please note, however, that in other contexts, "biomarkers" may also include gene mutations.

Biomarker Testing
You may also hear the testing referred to as genomic testing, tumor testing, molecular testing, next-generation sequencing (NGS), and genomic profiling. Biomarker testing is a general category of testing that looks for mutations in cancer genes to identify potential treatment options.

Cells
Basic units that make up your body.

Clinical Trial
Process by which new potential treatments are studied and compared to existing treatment options.

Companion Diagnostic (CDx)
A diagnostic test required to determine the eligibility of a patient for the intended use of a corresponding treatment.

DNA
Instructs cells how to grow and divide; DNA mutations may lead to cancer growth.

Food and Drug Administration (FDA)
The official US government agency responsible for review and approval of drugs and diagnostic tests to determine their safety and effectiveness for the intended use in patients.

Foundation Medicine
Company that performs biomarker/genomic testing.

FoundationOne CDx
An FDA-approved companion diagnostic test developed by Foundation Medicine that analyzes a set of genes and biomarkers to identify potential treatment options for advanced cancer patients with solid tumors.

Genes
Segments of DNA where mutations may be found with genomic testing.

Genomic Findings
Mutations identified in your cancer's DNA that may be matched with targeted treatment options.

Genomic Testing
You may also hear the testing referred to as biomarker testing, tumor testing, molecular testing, next-generation sequencing (NGS), and genomic profiling. Genomic testing is a general category of testing that looks for mutations in cancer genes to identify potential treatment options.

Immunotherapy
A type of cancer treatment that helps the body's immune system attack cancer cells.

Microsatellite Instability (MSI)
A biomarker that may help predict benefit from immunotherapy. MSI refers to a type of instability in a tumor's DNA.

Mutations
Changes in the DNA that can impact cancer growth (also referred to as "alterations").

NCCN category
A designation from the National Comprehensive Cancer Network that helps your doctor decide if the treatment might be appropriate for you.

Targeted Therapy
A type of cancer treatment that attacks cancer cells with specific gene mutations.

Tumor
A mass within the body caused by abnormal growth of cells.

Tumor Mutational Burden (TMB)
A biomarker that may help predict response to immunotherapy. TMB is a measure of the frequency of mutations in your tumor's DNA.

Tumor type
The type of cancer (e.g., lung cancer, breast cancer, etc.).

FoundationOne® CDx is a test intended to help doctors identify which cancer patients may benefit from certain treatments or clinical trial options. Use of the test does not guarantee that you will be matched to a treatment or clinical trial, or that all relevant alterations will be detected. Some patients may require a biopsy, which could pose a risk. For the full product labeling, including indications for use and risk information, visit our website, StartWithStepOne.com

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