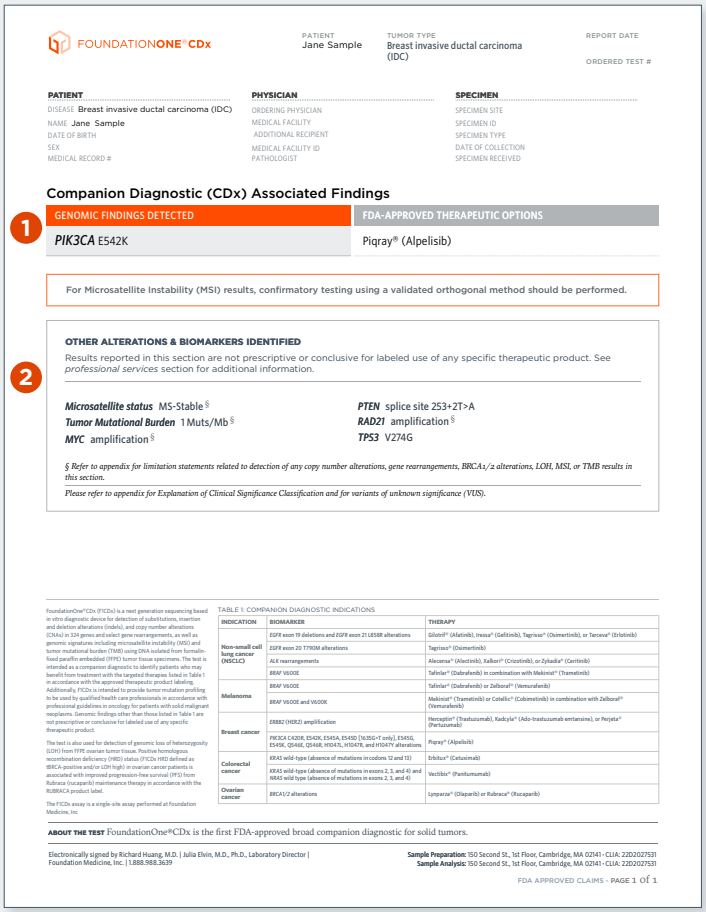
FOUNDATIONONE®CDx

Guide to FoundationOne®CDx Reports

Use this guide to learn about the key features of the FoundationOne CDx report

Section One: FDA-Approved Claims

Any FDA-approved claims will always appear at the beginning of the report, starting on page one.



FOUNDATIONONE®CDx

PATIENT Jane Sample | TUMOR TYPE Breast invasive ductal carcinoma (IDC) | REPORT DATE | ORDERED TEST #

PATIENT
DISEASE Breast invasive ductal carcinoma (IDC)
NAME Jane Sample
DATE OF BIRTH
SEX
MEDICAL RECORD #

PHYSICIAN
ORDERING PHYSICIAN
MEDICAL FACILITY
ADDITIONAL RECIPIENT
MEDICAL FACILITY ID
PATHOLOGIST

SPECIMEN
SPECIMEN SITE
SPECIMEN ID
SPECIMEN TYPE
DATE OF COLLECTION
SPECIMEN RECEIVED

Companion Diagnostic (CDx) Associated Findings

GENOMIC FINDINGS DETECTED	FDA-APPROVED THERAPEUTIC OPTIONS
PIK3CA E542K	Piqray® (Alpelisib)

1

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

2

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 1 Muts/Mb §
MYC amplification §
PTEN splice site 253+2T>A
RAD21 amplification §
TP53 V274G

§ 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 (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 benefit from treatment with the targeted therapies listed in Table 1 in accordance with the approved therapeutic product labeling. Additionally, F1CDx is intended to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with solid malignant neoplasms. Genomic findings other than those listed in Table 1 are not prescriptive or conclusive for labeled use of any specific therapeutic product.

The test is also used for detection of genomic loss of heterozygosity (LOH) from FFPE ovarian tumor tissue. Positive homologous recombination deficiency (HRD) status (F1CDx HRD defined as BRCA-positive and/or LOH high) in ovarian cancer patients is associated with improved progression-free survival (PFS) from Rubraca (rucaparib) maintenance therapy in accordance with the RUBRACA product label.

The F1CDx assay is a single-site assay performed at Foundation Medicine, Inc

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)
Melanoma	BRAF V600E	Tafinlar® (Dabrafenib) or Zelboraf® (Vemurafenib)
	BRAF V600E and V600K	Mekinist® (Trametinib) or Cotellic® (Cobimetinib) in combination with Zelboraf® (Vemurafenib)
Breast cancer	ERBB2 (HER2) amplification	Herceptin® (Trastuzumab), Kadcyla® (Ado-trastuzumab emtansine), or Perjeta® (Pertuzumab)
	PIK3CA C420R, E542K, E545A, E545D (K1352>T only), E545G, E545K, Q546E, Q546R, H1047L, H1047R, and H1047Y alterations	Piqray® (Alpelisib)
Colorectal cancer	KRAS wild-type (absence of mutations in codons 12 and 13)	Erbitux® (Cetuximab)
	KRAS wild-type (absence of mutations in exons 2, 3, and 4) and NRAS wild-type (absence of mutations in exons 2, 3, and 4)	Vectibix® (Panitumumab)
Ovarian cancer	BRCA1/2 alterations	Lynparza® (Olaparib) or Rubraca® (Rucaparib)

ABOUT THE TEST FoundationOne®CDx is the first FDA-approved broad companion diagnostic for solid tumors.

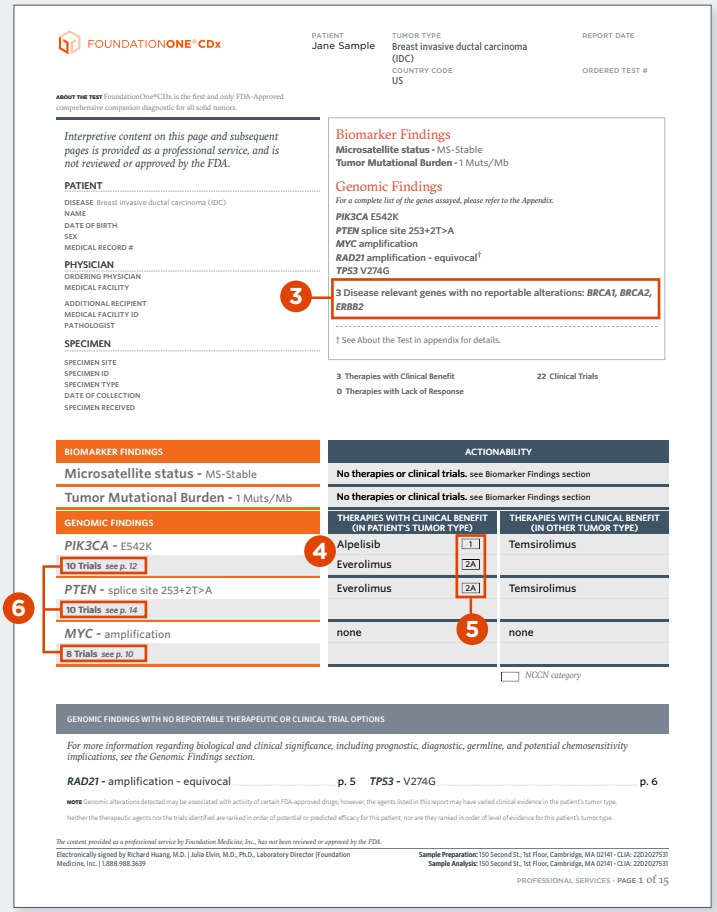
Electronically signed by Richard Huang, M.D. | Julia Elvin, M.D., Ph.D., Laboratory Director | Foundation Medicine, Inc. | 1.888.988.3639

Sample Preparation: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531
Sample Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 22D2027531

FDA APPROVED CLAIMS - PAGE 1 OF 1

Section Two: Professional Services

This section provides information about any biomarker and genomic findings.



FOUNDATIONONE®CDx

PATIENT Jane Sample | TUMOR TYPE Breast invasive ductal carcinoma (IDC) | COUNTRY CODE US | REPORT DATE | ORDERED TEST #

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.

PATIENT
DISEASE Breast invasive ductal carcinoma (IDC)
NAME
DATE OF BIRTH
SEX
MEDICAL RECORD #

PHYSICIAN
ORDERING PHYSICIAN
MEDICAL FACILITY
ADDITIONAL RECIPIENT
MEDICAL FACILITY ID
PATHOLOGIST

SPECIMEN
SPECIMEN SITE
SPECIMEN ID
SPECIMEN TYPE
DATE OF COLLECTION
SPECIMEN RECEIVED

Biomarker Findings
Microsatellite status - MS-Stable
Tumor Mutational Burden - 1 Muts/Mb

Genomic Findings
For a complete list of the genes assayed, please refer to the Appendix.
PIK3CA E542K
PTEN splice site 253+2T>A
MYC amplification
RAD21 amplification - equivocal†
TP53 V274G

3 Disease relevant genes with no reportable alterations: ***BRCA1, BRCA2, ERBB2***

† See About the Test in appendix for details.

3 Therapies with Clinical Benefit
0 Therapies with Lack of Response
22 Clinical Trials

BIOMARKER FINDINGS	ACTIONABILITY		
Microsatellite status - MS-Stable	No therapies or clinical trials. see Biomarker Findings section		
Tumor Mutational Burden - 1 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)**
PIK3CA - E542K	4 Alpelisib	1	Temsirolimus
10 Trials see p. 12	Everolimus	2A	
PTEN - splice site 253+2T>A	Everolimus	2A	Temsirolimus
10 Trials see p. 14			
MYC - amplification	none		none
8 Trials see p. 10			

6 5 NCCN category

GENOMIC FINDINGS WITH NO REPORTABLE THERAPEUTIC OR CLINICAL TRIAL OPTIONS

For more information regarding biological and clinical significance, including prognostic, diagnostic, germline, and potential chemosensitivity implications, see the Genomic Findings section.

RAD21 - amplification - equivocal ..... p. 5 ***TP53*** - V274G ..... p. 6

NOTE Genomic alterations detected may be associated with activity of certain FDA-approved drugs; however, the agents listed in this report may have varied clinical evidence in the patient's tumor type.

Neither the therapeutic agents nor the trials identified are ranked in order of potential or predicted efficacy for this patient, nor are they ranked in order of level of evidence for this patient's tumor type.

The content provided as a professional service by Foundation Medicine, Inc., has not been reviewed or approved by the FDA.

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PROFESSIONAL SERVICES - PAGE 1 OF 15

1 FDA-Approved CDx Claims
List of FDA-approved companion diagnostics associated with your patient's findings.

2 All Other Biomarkers and Genomic Signatures
All other genomic and biomarker findings, including microsatellite instability (MSI), tumor mutational burden (TMB), and Loss of heterozygosity (LOH, in ovarian cancer only), without companion diagnostic claims.

3 Pertinent Negatives
Identifies important negative results that can be used for patient management.

4 Therapies with Clinical Benefit
Therapies for each associated genomic finding are listed in alphabetic order. On the left are therapies within your patient's tumor type, and on the right are those with proven clinical benefit in other tumor types.

5 NCCN Categories of Evidence and Consensus
Associated NCCN Category that has been assigned to the therapy listed within your patient's tumor type.

6 Clinical Trials
Identifies trials based on your patient's unique genomic profile with page number for quick reference.

Note: The images shown on this piece are of a sample report and do not represent actual test results. This piece is intended to educate healthcare providers on the FoundationOne®CDx report and should not be used for patient diagnosis or treatment decisions.

Sample report images last updated April 2020.

Professional Services Continued

Detailed Information on Biomarker and Genomic Findings

Following the initial pages of the report, the professional services section goes into more detail about your patient's findings. Detailed information about their biomarker findings will appear first, followed by their genomic findings.

Potential Germline Findings
Alteration-specific text based on ClinVar pathogenic/likely pathogenic status for select genes* will appear here with a recommendation for follow-up germline testing.

Report Interpretation Services

For providers who have access to the Foundation Medicine portal, select the "Ask An Expert" button for additional help with report interpretation.

* The list of genes is based on professional guidelines from ACMG (Kalia et al., 2017; 27854360) and ESMO (Mandelker et al., 2019; 31050713). Gene list includes the following: *APC, BRCA1, BRCA2, BRIP1, MEN1, MLH1, MSH2, MSH6, MUTYH, NF2, PALB2, PMS2, PTEN, RAD51C, RAD51D, RB1, RET, SDHA, SDHB, SDHC, SDHD, SMAD4, STK11, TGFBR2, TP53, TSC1, TSC2, VHL, WT1.*

TO LEARN MORE:

Visit www.foundationmedicine.com/f1cdx

TO ORDER:

Create an account to order online at www.foundationmedicine.com/login

FoundationOne®CDx is a next-generation sequencing based *in vitro* test intended for use by healthcare professionals for advanced cancer patients with solid tumors. The test analyzes 324 genes as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB) and is FDA-approved as a companion diagnostic to identify patients who may benefit from treatment with a specific list of therapies (listed in Table 1 in the Technical Information at *http://www.foundationmedicine.com/f1cdx*) in accordance with the approved therapeutic product labeling. Additional genomic findings, other than those listed in Table 1, may be reported and are not prescriptive or conclusive for labeled use of any specific therapeutic product. Use of the test does not guarantee a patient will be matched to a treatment or clinical trial option, or that all relevant alterations will be detected. Some patients may require a biopsy. For the complete label, including important risk information, please visit *http://www.foundationmedicine.com/f1cdx*.

FOUNDATION MEDICINE®

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