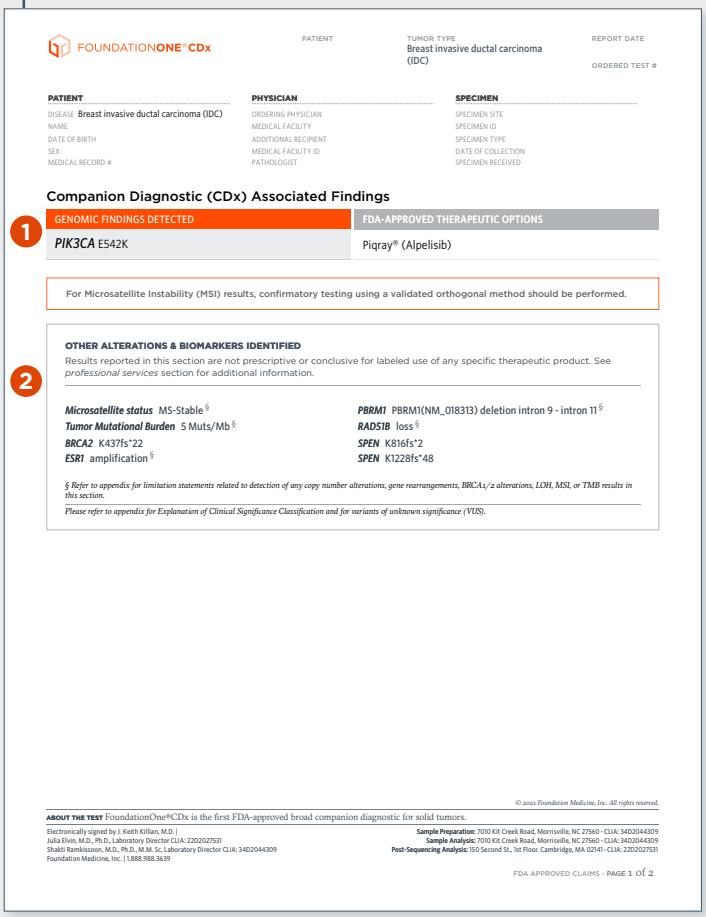
FOUNDATIONONE®CDx FOUNDATIONONE®LIQUID CDx

Guide to FoundationOne®CDx and FoundationOne®Liquid CDx Reports

FDA-Approved Claims

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



FOUNDATIONONE®CDx

PATIENT

TUMOR TYPE
Breast invasive ductal carcinoma (IDC)

REPORT DATE

ORDERED TEST #

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

Companion Diagnostic (CDx) Associated Findings

1

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

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 5 Muts/Mb §
BRCA2 K437fs*22
ESR1 amplification §
PBRM1 PBRM1(NM_018313) deletion intron 9 - intron 11 §
RAD51B loss §
SPEN K816fs*2
SPEN K1228fs*48

§ 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).

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

Electronically signed by J. Keith Killian, M.D. |
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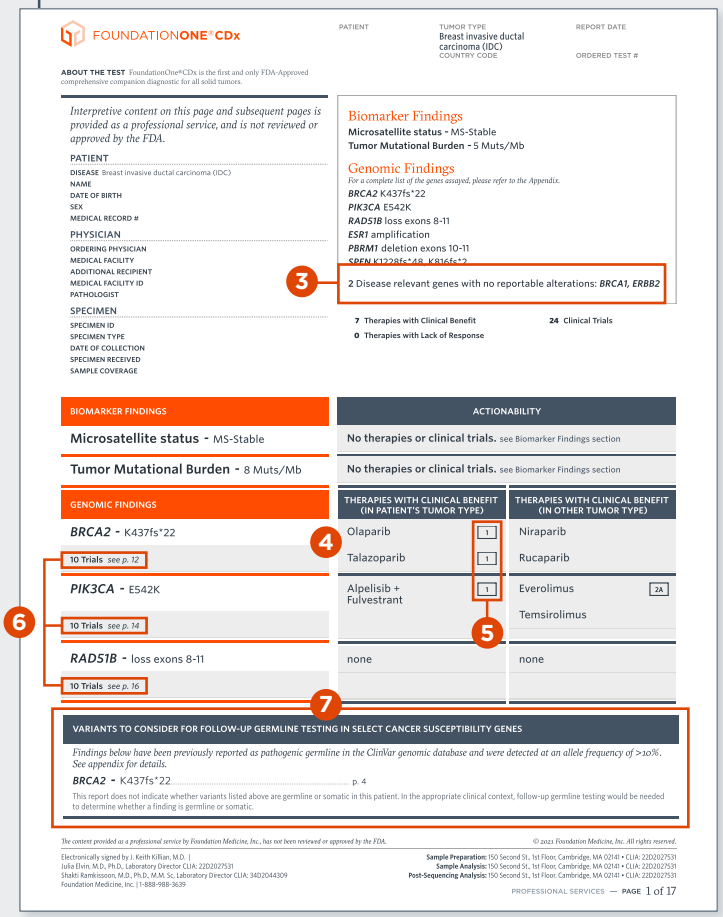
Post-Sequencing Analysis: 150 Second St., 1st Floor. Cambridge, MA 02141 • CLIA: 22D2027531

Professional Services

The Professional Services section provides information for all reported biomarker and genomic findings. This section is not reviewed or approved by the FDA.



FOUNDATIONONE®CDx

PATIENT

TUMOR TYPE
Breast invasive ductal carcinoma (IDC)
COUNTRY CODE

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 ID
SPECIMEN TYPE
DATE OF COLLECTION
SPECIMEN RECEIVED
SAMPLE COVERAGE

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

Genomic Findings
For a complete list of the genes assayed, please refer to the Appendix.
BRCA2 K437fs*22
PIK3CA E542K
RAD51B loss exons 8-11
ESR1 amplification
PBRM1 deletion exons 10-11
SPEN K1228fs*48, K816fs*2

3 2 Disease relevant genes with no reportable alterations: *BRCA1, ERBB2*

7 Therapies with Clinical Benefit
0 Therapies with Lack of Response
24 Clinical Trials

BIOMARKER FINDINGS	ACTIONABILITY
Microsatellite status - MS-Stable	No therapies or clinical trials. see Biomarker Findings section
Tumor Mutational Burden - 8 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)	
BRCA2 - K437fs*22	Olaparib	1	Niraparib	
10 Trials see p. 12	Talazoparib	1	Rucaparib	
PIK3CA - E542K	Alpelisib + Fulvestrant	1	Everolimus	2A
10 Trials see p. 14			Temsirolimus	
RAD51B - loss exons 8-11	none		none	
10 Trials see p. 16				

4 5 6 7

VARIANTS TO CONSIDER FOR FOLLOW-UP GERMLINE TESTING IN SELECT CANCER SUSCEPTIBILITY GENES

Findings below have been previously reported as pathogenic germline in the ClinVar genomic database and were detected at an allele frequency of >20%. See appendix for details.

BRCA2 - K437fs*22 ..... p. 4

This report does not indicate whether variants listed above are germline or somatic in this patient. In the appropriate clinical context, follow-up germline testing would be needed to determine whether a finding is germline or somatic.

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

2 Other Alterations and Biomarkers Identified
For FoundationOne CDx reports, all other genomic and biomarker findings without companion diagnostic claims will appear here. For FoundationOne Liquid CDx reports, alterations shown here are limited to short variants and select rearrangements and copy number alterations. The complete list of genomic and biomarker findings can be found in the Professional Services section.

3 Pertinent Negatives
Identifies important negative results that can be used for patient management. Pertinent negatives do not appear for FoundationOne Liquid CDx.

4 Therapies with Clinical Benefit
Therapies for each associated genomic finding are listed in the therapy table. 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. Therapy resistance based on your patient's genomic profile will also be indicated.

5 National Comprehensive Cancer Network® (NCCN®) Categories of Evidence and Consensus[1]
Associated NCCN Category that has been assigned to the therapy listed within your patient's tumor type.

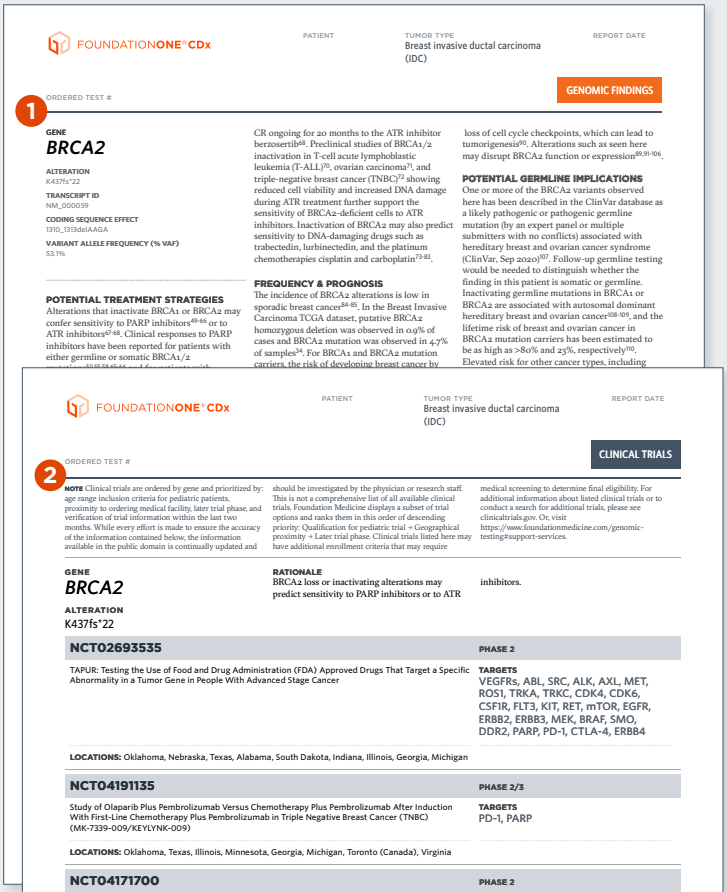
6 Clinical Trials
Identifies number of trials based on your patient's unique genomic profile with page number for quick reference.

7 Potential Germline Findings
Lists variants in select cancer susceptibility genes that have been previously reported as pathogenic or likely pathogenic in the ClinVar genomic database and are identified at an allele frequency that is plausible for potential germline origin for consideration of follow-up germline testing.

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

Sample report images last updated January 2021.

Professional Services Continued


FOUNDATIONONE®CDx

PATIENT

TUMOR TYPE
Breast invasive ductal carcinoma (IDC)

REPORT DATE

ORDERED TEST #

1

GENOMIC FINDINGS

GENE
BRCA2

ALTERATION
K437fs*22

TRANSCRIPT ID
NM_000059

CODING SEQUENCE EFFECT
1310_1313delAAGA

VARIANT ALLELE FREQUENCY (% VAF)
53.1%

POTENTIAL TREATMENT STRATEGIES
Alterations that inactivate BRCA1 or BRCA2 may confer sensitivity to PARP inhibitors[49-66] or to ATR inhibitors[67-68]. Clinical responses to PARP inhibitors have been reported for patients with either germline or somatic BRCA1/2

CR ongoing for 20 months to the ATR inhibitor berzosertib[68]. Preclinical studies of BRCA1/2 inactivation in T-cell acute lymphoblastic leukemia (T-ALL)[70], ovarian carcinoma[71], and triple-negative breast cancer (TNBC)[72] showing reduced cell viability and increased DNA damage during ATR treatment further support the sensitivity of BRCA2-deficient cells to ATR inhibitors. Inactivation of BRCA2 may also predict sensitivity to DNA-damaging drugs such as trabectedin, lurbinectedin, and the platinum chemotherapies cisplatin and carboplatin[73-83].

FREQUENCY & PROGNOSIS
The incidence of BRCA2 alterations is low in sporadic breast cancer[84-85]. In the Breast Invasive Carcinoma TCGA dataset, putative BRCA2 homozygous deletion was observed in 0.9% of cases and BRCA2 mutation was observed in 4.7% of samples[34]. For BRCA1 and BRCA2 mutation carriers, the risk of developing breast cancer by

loss of cell cycle checkpoints, which can lead to tumorigenesis[80]. Alterations such as seen here may disrupt BRCA2 function or expression[88,91-106].

POTENTIAL GERMLINE IMPLICATIONS
One or more of the BRCA2 variants observed here has been described in the ClinVar database as a likely pathogenic or pathogenic germline mutation (by an expert panel or multiple submitters with no conflicts) associated with hereditary breast and ovarian cancer syndrome (ClinVar, Sep 2020)[107]. Follow-up germline testing would be needed to distinguish whether the finding in this patient is somatic or germline. Inactivating germline mutations in BRCA1 or BRCA2 are associated with autosomal dominant hereditary breast and ovarian cancer[108-109], and the lifetime risk of breast and ovarian cancer in BRCA2 mutation carriers has been estimated to be as high as >80% and 25%, respectively[110]. Elevated risk for other cancer types, including

FOUNDATIONONE®CDx

PATIENT

TUMOR TYPE
Breast invasive ductal carcinoma (IDC)

REPORT DATE

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2

CLINICAL TRIALS

NOTE 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
BRCA2

ALTERATION
K437fs*22

RATIONALE
BRCA2 loss or inactivating alterations may predict sensitivity to PARP inhibitors or to ATR inhibitors.

NCT02693535	**PHASE 2**
TAPUR: Testing the Use of Food and Drug Administration (FDA) Approved Drugs That Target a Specific Abnormality in a Tumor Gene in People With Advanced Stage Cancer	**TARGETS** VEGFRs, ABL, SRC, ALK, AXL, MET, ROS1, TRKA, TRKC, CDK4, CDK6, CSF1R, FLT3, KIT, RET, mTOR, EGFR, ERBB2, ERBB3, MEK, BRAF, SMO, DDR2, PARP, PD-1, CTLA-4, ERBB4
LOCATIONS: Oklahoma, Nebraska, Texas, Alabama, South Dakota, Indiana, Illinois, Georgia, Michigan	
NCT04191135	**PHASE 2/3**
Study of Olaparib Plus Pembrolizumab Versus Chemotherapy Plus Pembrolizumab After Induction With First-Line Chemotherapy Plus Pembrolizumab in Triple Negative Breast Cancer (TNBC) (MK-7339-009/KEYLYNK-009)	**TARGETS** PD-1, PARP
LOCATIONS: Oklahoma, Texas, Illinois, Minnesota, Georgia, Michigan, Toronto (Canada), Virginia	
NCT04171700	**PHASE 2**
A Study to Evaluate Rucaparib in Patients With Solid Tumors and With Deleterious Mutations in HRR Genes	**TARGETS** PARP
LOCATIONS: Oklahoma, Texas, Iowa, Tennessee, Illinois, Minnesota, Pennsylvania, Florida	
NCT04041128	**PHASE NULL**
PARP Inhibition During Pre-surgical Window in Breast/Ovary Cancer	**TARGETS** PARP
LOCATIONS: Texas	
NCT02849496	**PHASE 2**
Olaparib With or Without Atezolizumab in Treating Patients With Locally Advanced or Metastatic Non-HER2-Positive Breast Cancer	**TARGETS** PD-L1, PARP
LOCATIONS: Texas, Missouri, Tennessee, Illinois, Minnesota, Colorado	

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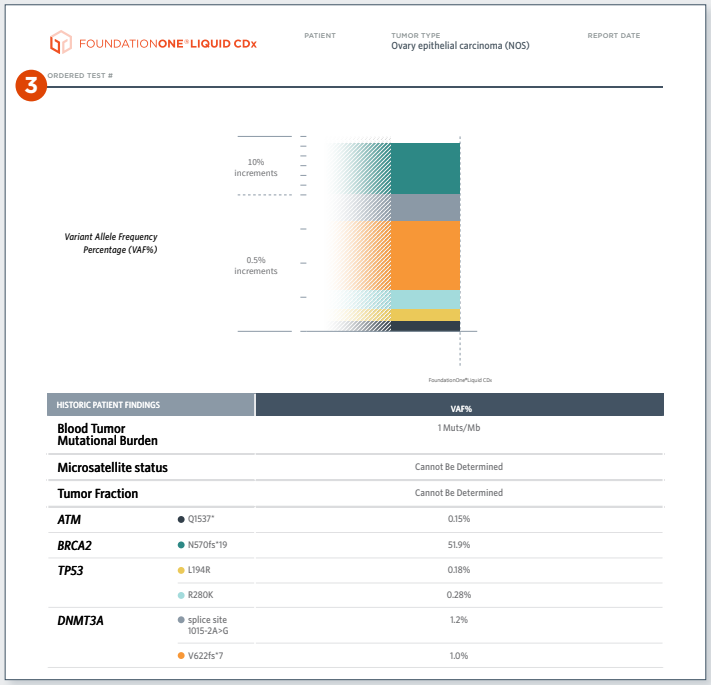
PROFESSIONAL SERVICES - PAGE 12 OF 17


FOUNDATIONONE®LIQUID CDx

PATIENT

TUMOR TYPE
Ovary epithelial carcinoma (NOS)

REPORT DATE

ORDERED TEST #

3

HISTORIC PATIENT FINDINGS		VAF%
Blood Tumor Mutational Burden		1 Muts/Mb
Microsatellite status		Cannot Be Determined
Tumor Fraction		Cannot Be Determined
ATM	Q1537*	0.15%
BRCA2	N570fs*19	51.9%
TP53	L194R	0.18%
	R280K	0.28%
DNMT3A	splice site 1015-2A>G	1.2%
	V622fs*7	1.0%

1 Biomarker and Genomic Findings
Following the initial pages of the report, the professional services section goes into more detail about your patient's findings.

2 Clinical Trial Information
Detailed information about the clinical trials your patient has been matched to, ranked for the patient based on location and trial phase.

3 FoundationOne Liquid CDx Variant Allele Frequency Percentage (VAF%) Graph and Table
Shows the detected VAF% and where applicable in the patient's biomarkers and/or genomic signatures. Up to 5 previous tests may be shown. For FoundationOne CDx reports, VAF values are displayed in the Genomic Findings section of Professional Services, alongside other variant information.

Medical Case Consulting
For additional help with report interpretation, select the "Ask An Expert" feature on your provider portal or contact client services at (888) 988-3639.

To learn more about our FDA-approved portfolio, go to *foundationmedicine.com/portfolio*

1. Referenced with permission from the National Comprehensive Cancer Network, Inc. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. To view the most recent and complete version of the recommendations, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

FoundationOne®CDx and FoundationOne®Liquid CDx are qualitative next-generation sequencing based *in vitro* diagnostic tests for advanced cancer patients with solid tumors and are for prescription use only. FoundationOne CDx utilizes FFPE tissue and analyzes 324 genes as well as genomic signatures. FoundationOne Liquid CDx analyzes 324 genes utilizing circulating cell-free DNA and is FDA-approved to report short variants in 311 genes. The tests are companion diagnostics to identify patients who may benefit from treatment with specific therapies in accordance with the therapeutic product labeling. Additional genomic findings may be reported and are not prescriptive or conclusive for labeled use of any specific therapeutic product. Use of the tests does not guarantee a patient will be matched to a treatment. A negative result does not rule out the presence of an alteration. Some patients may require a biopsy for testing with FoundationOne CDx when archival tissue is not available which may pose a risk. Patients who are tested with FoundationOne Liquid CDx and are negative for companion diagnostic mutations should be reflexed to tumor tissue testingand mutation status confirmed using an FDA-approved tumor tissue test, if feasible.

For the complete label, including companion diagnostic indications and important risk information, please visit www.F1CDxLabel.com and www.F1LCDxLabel.com.

FOUNDATION MEDICINE®

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