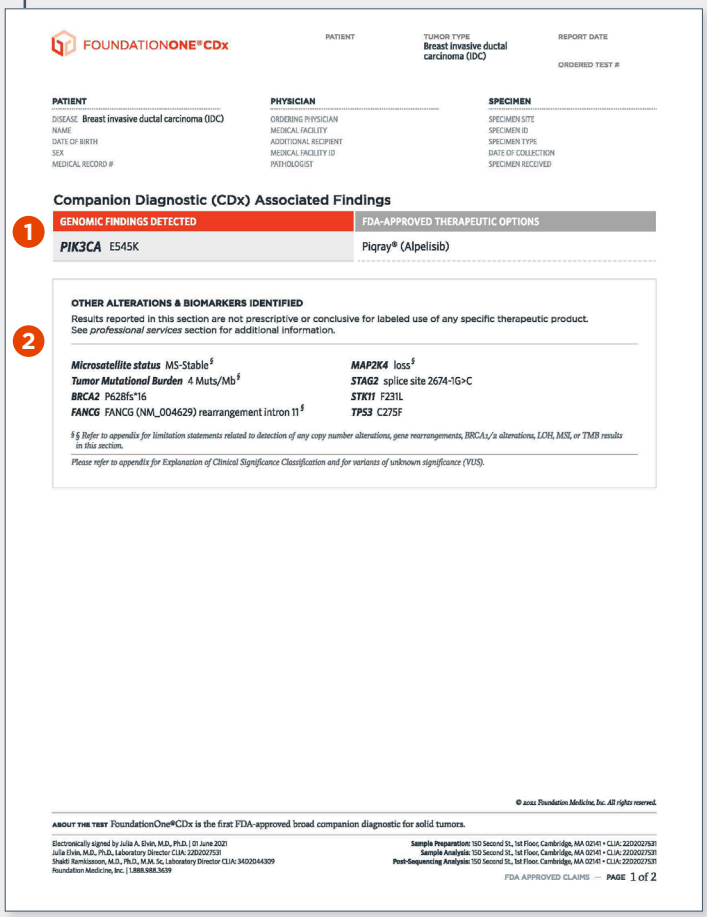
FOUNDATIONONE®CDx FOUNDATIONONE®LIQUID CDx

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 E545K	Piqray® (Alpelisib)

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 4 Muts/Mb§
BRCA2 P628fs*16
FANCG FANCG (NM_004629) rearrangement intron 11§
MAP2K4 loss§
STAG2 splice site 2674-1G>C
STK11 F231L
TP53 C275F

§§ *Refer to appendix for limitation statements related to detection of any copy number alterations, gene rearrangements, BRCAs/a 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 Julia A. Elvin, M.D., Ph.D. | 01 June 2021
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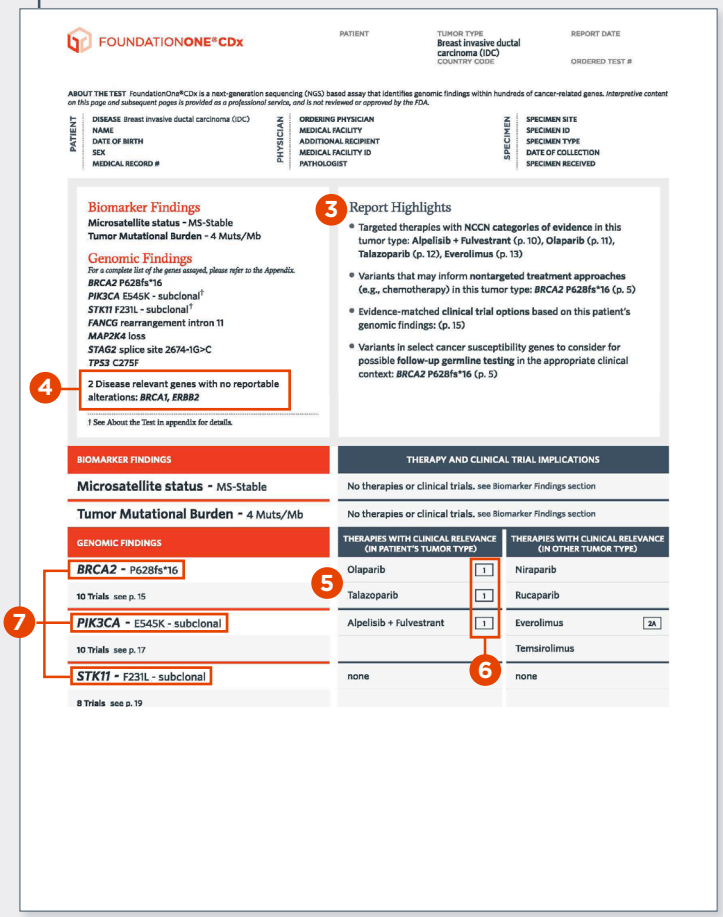
Post-Sequencing Analysis: 150 Second St., 1st Floor, Cambridge, MA 02141 • CLIA: 2202027531

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 a next-generation sequencing (NGS) based assay that identifies genomic findings within hundreds of cancer-related genes. *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 - 4 Muts/Mb

Genomic Findings
For a complete list of the genes assayed, please refer to the Appendix.
BRCA2 P628fs*16
PIK3CA E545K - subclonal†
STK11 F231L - subclonal†
FANCG rearrangement intron 11
MAP2K4 loss
STAG2 splice site 2674-1G>C
TP53 C275F

4 2 Disease relevant genes with no reportable alterations: ***BRCA1, ERBB2***

† See About the Test in appendix for details.

3 **Report Highlights**
- Targeted therapies with **NCCN categories of evidence** in this tumor type: **Alpelisib + Fulvestrant** (p. 10), **Olaparib** (p. 11), **Talazoparib** (p. 12), **Everolimus** (p. 13)
- Variants that may inform **nontargeted treatment approaches** (e.g., chemotherapy) in this tumor type: ***BRCA2*** **P628fs*16** (p. 5)
- Evidence-matched **clinical trial options based on this patient's genomic findings:** (p. 15)
- Variants in select cancer susceptibility genes to consider for possible **follow-up germline testing** in the appropriate clinical context: ***BRCA2*** **P628fs*16** (p. 5)

BIOMARKER FINDINGS	THERAPY AND CLINICAL TRIAL IMPLICATIONS	
Microsatellite status - MS-Stable	No therapies or clinical trials. see Biomarker Findings section	
Tumor Mutational Burden - 4 Muts/Mb	No therapies or clinical trials. see Biomarker Findings section	
GENOMIC FINDINGS	THERAPIES WITH CLINICAL RELEVANCE (IN PATIENT'S TUMOR TYPE)	THERAPIES WITH CLINICAL RELEVANCE (IN OTHER TUMOR TYPE)
BRCA2 - P628fs*16	Olaparib 1	Niraparib
10 Trials see p. 15	5 Talazoparib 1	Rucaparib
7 ***PIK3CA*** - E545K - subclonal	Alpelisib + Fulvestrant 1	Everolimus 2A
10 Trials see p. 17		Temsirolimus
STK11 - F231L - subclonal	none 6	none
8 Trials see p. 19		

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 Report Highlights
This feature distills important genomic insights in one easy-to-find place, helping you focus on the key actionable results to inform your patient's treatment plan.

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

5 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.

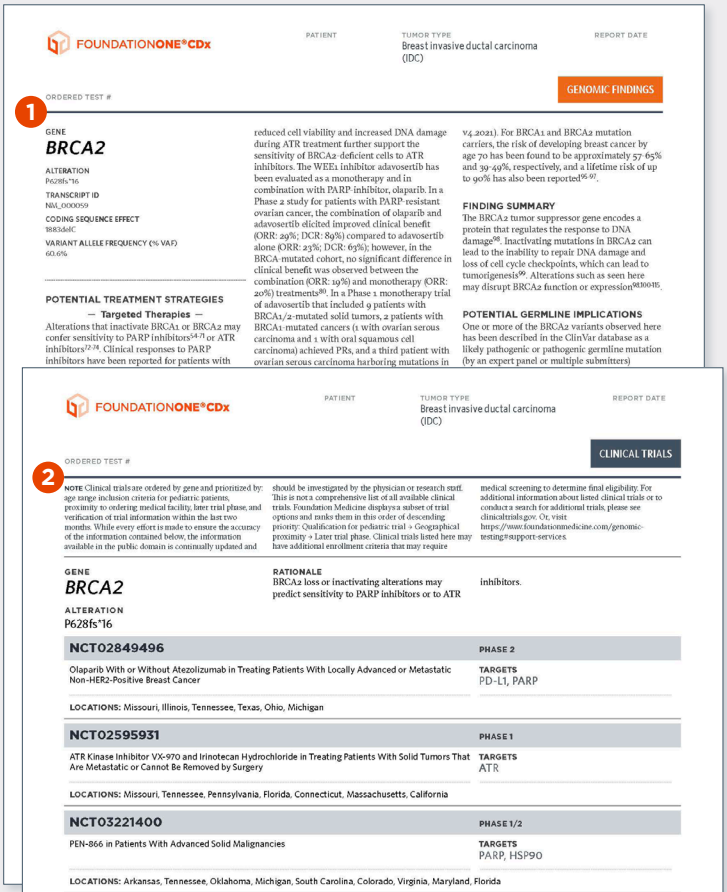
6 National Comprehensive Cancer Network® (NCCN®) Categories of Evidence and Consensus[1]
Associated NCCN Category that has been assigned to the therapy listed within your patient's tumor type.

7 Clinical Trials
Identifies number of 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 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 December 2021.

Professional Services Continued


FOUNDATIONONE®CDx

PATIENT

TUMOR TYPE
Breast invasive ductal carcinoma (IDC)

REPORT DATE

ORDERED TEST #

1

GENOMIC FINDINGS

GENE
BRCA2

ALTERATION
P628fs*16

TRANSCRIPT ID
NM_000059

CODING SEQUENCE EFFECT
1883delC

VARIANT ALLELE FREQUENCY (% VAF)
60.6%

POTENTIAL TREATMENT STRATEGIES

— Targeted Therapies —

Alterations that inactivate BRCA1 or BRCA2 may confer sensitivity to PARP inhibitors[94,95] or ATR inhibitors[97,98]. Clinical responses to PARP inhibitors have been reported for patients with

reduced cell viability and increased DNA damage during ATR treatment further support the sensitivity of BRCA2-deficient cells to ATR inhibitors. The WEE1 inhibitor adavosertib has been evaluated as a monotherapy and in combination with PARP inhibitor, olaparib. In a Phase 2 study for patients with PARP-resistant ovarian cancer, the combination of olaparib and adavosertib elicited improved clinical benefit (ORR: 29%; DCR: 89%) compared to adavosertib alone (ORR: 23%; DCR: 63%); however, in the BRCA-mutated cohort, no significant difference in clinical benefit was observed between the combination (ORR: 19%) and monotherapy (ORR: 20%) treatments[96]. In a Phase 1 monotherapy trial of adavosertib that included 9 patients with BRCA1/2-mutated solid tumors, 2 patients with BRCA1-mutated cancers (1 with ovarian serous carcinoma and 1 with oral squamous cell carcinoma) achieved PRs, and a third patient with ovarian serous carcinoma harboring mutations in

v4.2021). For BRCA1 and BRCA2 mutation carriers, the risk of developing breast cancer by age 70 has been found to be approximately 57-65% and 39-49%, respectively, and a lifetime risk of up to 90% has also been reported[96,97].

FINDING SUMMARY

The BRCA2 tumor suppressor gene encodes a protein that regulates the response to DNA damage[98]. Inactivating mutations in BRCA2 can lead to the inability to repair DNA damage and loss of cell cycle checkpoints, which can lead to tumorigenesis[99]. Alterations such as seen here may disrupt BRCA2 function or expression[98,100-115].

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)

FOUNDATIONONE®CDx

PATIENT

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Breast invasive ductal carcinoma (IDC)

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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
P628fs*16

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

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: Missouri, Illinois, Tennessee, Texas, Ohio, Michigan	
NCT02595931	PHASE 1
ATR Kinase Inhibitor VX-970 and Irinotecan Hydrochloride in Treating Patients With Solid Tumors That Are Metastatic or Cannot Be Removed by Surgery	TARGETS ATR
LOCATIONS: Missouri, Tennessee, Pennsylvania, Florida, Connecticut, Massachusetts, California	
NCT03221400	PHASE 1/2
PEN-866 in Patients With Advanced Solid Malignancies	TARGETS PARP, HSP90
LOCATIONS: Arkansas, Tennessee, Oklahoma, Michigan, South Carolina, Colorado, Virginia, Maryland, Florida	
NCT04041128	PHASE NULL
PARP Inhibition During Pre-surgical Window in Breast/Ovary Cancer	TARGETS PARP
LOCATIONS: Texas	
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, Illinois, Texas, Minnesota, Michigan, Georgia, Toronto (Canada)	

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

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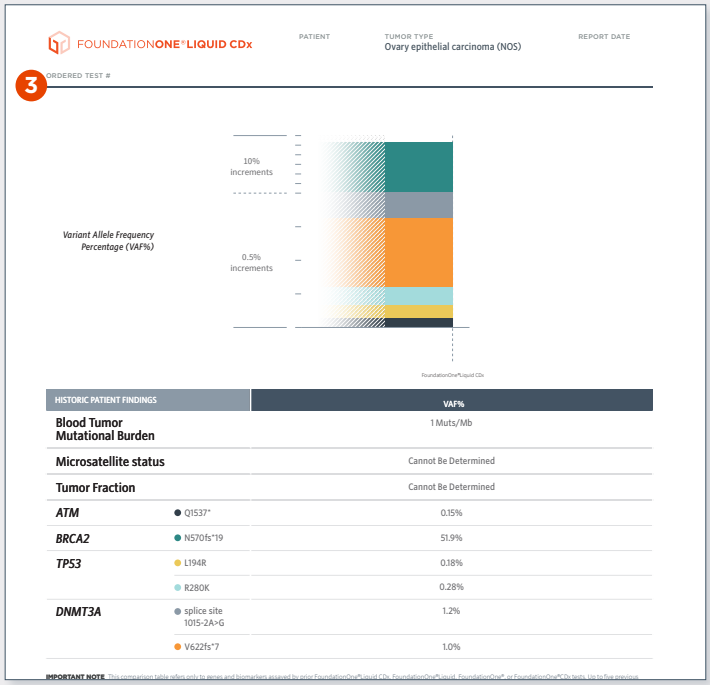
FOUNDATIONONE®LIQUID CDx

PATIENT

TUMOR TYPE
Ovary epithelial carcinoma (NOS)

REPORT DATE

ORDERED TEST #

3

Variant Allele Frequency Percentage (VAF%)

10% increments

0.5% increments

FoundationOne®Liquid CDx

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%

IMPORTANT NOTE This comparison table refers only to genes and biomarkers assayed by prior FoundationOne®Liquid CDx, FoundationOne®Liquid, FoundationOne®, or FoundationOne®CDx tests. Up to five previous

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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