FOUNDATIONONE® CDx

Frequently Asked Questions

About the First FDA-Approved Broad Companion Diagnostic (CDx) Test for Solid Tumors

What is FoundationOne®CDx?

FoundationOne CDx is the first FDA-approved broad companion diagnostic for solid tumors, featuring simplified reporting and national coverage[1] for qualifying Medicare and Medicare Advantage patients.

FoundationOne CDx is approved for use by the FDA for all solid tumors. It is intended for use by physicians as a companion diagnostic test to identify patients that may benefit from treatment following detection of specific genomic findings in approved indications – including non-small cell lung cancer (NSCLC), colorectal cancer (CRC), melanoma, breast cancer and ovarian cancer – and to provide tumor mutation profiling to be used by providers according to professional guidelines in oncology.

- FoundationOne CDx is a next generation sequencing based *in vitro* diagnostic device for detection of substitutions, insertion and deletion alterations, and copy number alterations 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 also used for detection of genomic loss of heterozygosity (LOH) from formalin-fixed, paraffinembedded (FFPE) ovarian tumor tissue. Positive homologous recombination deficiency (HRD) status (defined as tBRCA-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 platform employs whole-genome shotgun library construction and hybridization-based capture of DNA extracted from FFPE tumor tissue prior to uniform and deep sequencing on the Illumina® HiSeq® 4000. Following sequencing, custom software is used to determine genomic variants including substitutions, insertion and deletion variants (indels), copy number alterations (CNAs), genomic rearrangements, microsatellite instability (MSI) and tumor mutational burden (TMB). The output of the test includes:
  - **Category 1:** Companion Diagnostic (CDx) Claims noted in Table 1 of the Intended Use
  - **Category 2:** Cancer Mutations with Evidence of Clinical Significance
  - **Category 3:** Cancer Mutations with Potential Clinical Significance

How is FoundationOne CDx different from FoundationOne?

- **Regulatory Status:** FoundationOne CDx is the next evolution of FoundationOne, our pioneering laboratory-developed test (LDT). FoundationOne CDx is approved by the FDA. FoundationOne is performed in our CLIA-certified and CAP-accredited laboratory.
- **Coverage:** FoundationOne CDx has national coverage for qualifying Medicare and Medicare Advantage patients across all solid tumors.[1]
- **Simplified Report:** FoundationOne CDx has a simplified report format with all alterations on Page 1, including alterations associated with companion diagnostic claims that inform eligibility for associated therapies and other tumor-profiling results that can be used for treatment management according to professional guidelines in oncology. There are three sections of the FoundationOne CDx report: 1) FDA-Approved Content, 2) Professional Services and 3) Appendix.
- **Clinical Validation:** FoundationOne CDx has been clinically and analytically validated – with 9x more samples and cell lines validated for FoundationOne CDx as compared with FoundationOne, which is analytically validated.[2]

What risks might be associated with the test?

Alterations reported may include somatic (not inherited) or germline (inherited) alterations; however, the test does not distinguish between germline and somatic alterations. The test does not provide information about susceptibility. Biopsy may pose a risk to the patient when archival tissue is not available for use with the assay. The patient's physician should determine whether the patient is a candidate for biopsy. Reflex testing to an alternative FDA-approved companion diagnostic should be performed for patients who have an ERBB2 amplification result detected with copy number equal to 4 (baseline ploidy of tumor +2) for confirmatory testing. While this result is considered negative by F1CDx, in a clinical

concordance study with an FDA-approved FISH test, 70% (7 out of 10 samples) were positive, and 30% (3 out 10 samples) were negative by the FISH test with an average ratio of 2.3. The frequency of ERBB2 copy number 4 in breast cancer is estimated to be approximately 2%.[3] See Technical Information for additional information on assay limitations, ***www.foundationmedicine.com/f1cdx.***

How to order the FoundationOne®CDx test and obtain results

How do I order the test?

Order online by signing up for a Foundation Medicine account at ***https://home.foundationmedicine.com/signup*** or order by fax or email by downloading the test requisition form and faxing the completed form, along with the patient's pathology report and insurance information, to 617.418.2290.

How long does it take to get a result?

Results will be available in less than two weeks from the time Foundation Medicine receives the tissue sample.

What are the specimen guidelines?

To obtain the full specimen guidelines, visit ***www.foundationmedicine.com/f1cdx***, call our Client Services team at 888.988.3639 or contact your local Foundation Medicine sales representative.

Whom can I speak to about the result?

Healthcare providers can call Foundation Medicine at 888.988.3639 to speak with our client services team (Hours of operation: Monday through Friday, 8 a.m. to 8 p.m. ET).

Is FoundationOne CDx covered by insurance?

- For qualifying Medicare and Medicare Advantage patients, coverage for FoundationOne CDx may be available[1], minus any applicable co-insurance and/or deductible amounts.
- Foundation Medicine accepts all insurance plans; however, we are currently out-of-network providers with most commercial insurance plans.

About Foundation Medicine

Who is Foundation Medicine?

Foundation Medicine is a world-leading molecular insights company offering a suite of testing and support services to connect physicians and their patients to the latest cancer treatment approaches and making precision medicine a reality for thousands. For more information, please visit foundationmedicine.com or follow us on Twitter (@FoundationATCG).

TO LEARN MORE:	TO ORDER:
Visit www.foundationmedicine.com/f1cdx	Create an account to order online at www.foundationmedicine.com/signup

References

1. Medicare and Medicare Advantage members have coverage of FoundationOne CDx in accordance with the Centers for Medicare and Medicaid Services (CMS) national coverage determination (NCD) criteria. **2.** Frampton et al. "Development and validation of a clinical cancer genomic profiling test based on massively parallel DNA sequencing. Nature Biotechnology: 31(11):1023-1031. November 2013. **3.** Multiple references listed in https://www.mycancergenome.org/content/disease/breast-cancer/ERBB2/238/ report the frequency of HER2 overexpression as 20% in breast cancer. Based on the F1CDx HER2 CDx concordance study, approximately 10% of HER2 amplified samples had copy number 4. Thus, total frequency is conservatively estimated to be approximately 2%.

FOUNDATION MEDICINE®

www.foundationmedicine.com | Tel. 888.988.3639 | Fax 617.418.2290 | MKT-0141-04