Physician Insert: oncoReveal® CDx

FOR IN VITRO DIAGNOSTIC USE
Caution: Federal law restricts this device to sale by or on the order of a physician

Genetic Companion Diagnostic Test For Targeted Therapy Selection in Non-Small Cell Lung Cancer (NSCLC) and Colorectal Cancer (CRC)

For the most current information on the association of the biomarker and therapeutic outcomes, refer to the therapeutic labels available at Drugs@FDA on the FDA website.

Intended Use/Indications For Use

The oncoReveal® CDx is a qualitative next generation sequencing based *in vitro* diagnostic test that uses amplicon-based target enrichment technology for detection of single nucleotide variants (SNVs), insertions and deletions in 22 genes using DNA isolated from formalin-fixed paraffin-embedded (FFPE) tumor tissue specimens and using the Illumina MiSeqDx®. 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, oncoReveal® CDx is intended to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for previously diagnosed cancer 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.

Table 1 List of Somatic Variants for Therapeutic Use

Indication	Gene	Variant	Targeted therapy
Colorectal Cancer (CRC)	KRAS	KRAS wild-type (absence of mutations in codons 12 and 13)	ERBITUX® (cetuximab), or VECTIBIX® (panitumumab)
Non-Small Cell Lung Cancer (NSCLC)	*EGFR*	Exon 19 In Frame Deletions and Exon 21 L858R Substition Mutations	EGFR Tyrosine Kinase Inhibitors approved by FDA*

* For the most current information about the therapeutic products in this group, go to: https://www.fda.gov/medicaldevices/productsandmedicalprocedures/invitrodiagnostics/ucm301431.htm

Test Overview

In addition to the companion diagnostic (CDx) claims noted in Table 1 of the intended use/indications for use, the oncoReveal® CDx also reports SNV, insertions and deletion of the 22 genes listed Table 2 to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for previously diagnosed cancer patients with solid malignant neoplasms.

Table 2 Genes targeted by the oncoReveal® CDx for the detection of SNVs, insertions and deletions.

AKT1	*CTNNB1*	*ERBB2*	*FGFR1*	*KRAS*	*NOTCH1*	*PTEN*	*TP53*
ALK	*DDR2*	*ERBB4*	*FGFR2*	*MAP2K1*	*NRAS*	*SMAD4*	
BRAF	*EGFR*	*FBXW7*	*FGFR3*	*MET*	*PIK3CA*	*STK11*	

Guide to the Interpretation of Test Results

Genomic findings other than those listed in Table 1 are not prescriptive or conclusive for labeled use of any specific therapeutic product.

Test results should be interpreted in the context of pathological evaluation of tumors, treatment history, clinical findings, and other laboratory data.

The test report includes genomic finding reported in the following levels:

Level 1: Companion Diagnostic Claims noted in Table 1 of the oncoReveal® CDx Intended Use/Indications for Use

Companion diagnostics (CDx) claims listed in Table 1 of the oncoReveal® CDx Intended Use/Indications for Use provide information that is essential for the safe and effective use of a corresponding therapeutic product, such as a drug. CDx claims in Table 1 are supported by analytical performance of the test for each specific biomarker and a clinical study establishing either the link between the result of that test and patient outcomes or clinical concordance to a previously approved CDx.

Level 2: Cancer Mutations with Evidence of Clinical Significance

Biomarkers reported by the oncoReveal® CDx described as cancer mutations with evidence of clinical significance enable health care professionals to use information about their patients' tumors in accordance with the clinical evidence, such as clinical evidence presented in professional guidelines, as appropriate. Such claims are supported by a demonstration of analytical performance and clinical validity (typically based on publicly available clinical evidence, such as professional guidelines and/or peer-reviewed publications). Genomic findings reported by the oncoReveal® CDx described as cancer mutations with evidence of clinical significance are not prescriptive or conclusive for labeled use of any specific therapeutic product.

Level 3: Cancer Mutations with Potential Clinical Significance

Mutations not considered biomarkers in Level 1 or Level 2 reported by the oncoReveal® CDx described as cancer mutations with potential clinical significance may be informational or used to direct patients towards clinical trials for which they may be eligible. Such claims are supported by analytical performance, and clinical or mechanistic rationale for inclusion in the panel. Such rationales would include peer-reviewed publications or in vitro pre-clinical models. Genomic findings reported by the oncoReveal® CDx described as cancer mutations with potential clinical significance are not prescriptive or conclusive for labeled use of any specific therapeutic product.

Test Limitations

1. The oncoReveal® CDx has only been validated for CDx use with CRC and NSCLC tumor tissues. Test only the indicated tissue types.
2. The oncoReveal® CDx has only been validated for pan cancer tumor profiling for solid malignant neoplasms.
3. Genomic findings reported by the oncoReveal® CDx described as Level 2: Cancer Mutations with Potential Clinical Significance or Level 3: Cancer Mutations with Potential Clinical Significance are not prescriptive or conclusive for labeled use of any specific therapeutic product.
4. The oncoReveal® CDx has been validated for use with genomic DNA extracted from FFPE tumor tissues. Other sample types or fixation methods have not been evaluated.
5. The oncoReveal® CDx has not been validated for use with fine needle aspirates (FNA) as a specimen type.
6. Targeted molecular testing can only provide information for the targeted regions. A negative test result cannot rule out the possibility of other mutations with clinical utility outside of the target region. For example, samples with results reported as “No mutation detected” may harbor *KRAS* and *EGFR* variants not reported by the assay.
7. A negative “No mutation detected” result does not rule out the presence of a mutation that may be present but below the limits of detection of this test (see Analytical Sensitivity: Limit of Detection section).
8. A “No Call” result for Level 2 and Level 3 variants are at risk of being false negative results.
9. Positive mutation Call for Level 2 and Level 3 variants may be at risk of being false positive calls since they may be reported when the variant does not meet coverage requirements.
10. This assay does not interrogate all variants or genes (*NRAS*) that confer resistance to cetuximab and panitumumab.
11. The oncoReveal® CDx is not to be used for diagnosis of any disease.
12. The oncoReveal® CDx is designed to report out somatic variants and is not intended to report germline variants. However, not all rare and novel germline variants, not listed in the germline database(s) may be filtered.

Patents and Trademarks

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