

Bruce, Wayne (A0126298)
Patient MRN: 987654321 | DOB: JAN-01-1976 | Sex: Male
Diagnosis: Non Small Cell Lung Cancer (NSCLC)



REPORTING		PHYSICIAN
Report Date:	MAR-20-2017	Dougie Houser
Receipt Date:	MAR-04-2017	Center for People Who are Sick and Want to Get Better
Collection Date:	MAR-03-2017	123 Four St., Metropolis, NY, 12345, USA
Specimen:	Blood	Ph: (808) 555-1234 Fax: N/A
Status:	FINAL	Additional Recipient: N/A

Companion Diagnostic

No reportable alterations with companion diagnostic (CDx) claims

Intended Use

Guardant360® CDx is a qualitative next generation sequencing-based in vitro diagnostic device that uses targeted high throughput hybridization-based capture technology for detection of single nucleotide variants (SNVs), insertions and deletions (indels) in 55 genes, copy number amplifications (CNAs) in two (2) genes, and fusions in four (4) genes. Guardant360 CDx utilizes circulating cell-free DNA (cfDNA) from plasma of peripheral whole blood collected in Streck Cell-Free DNA Blood Collection Tubes (BCTs). The test is intended to be used as a companion diagnostic to identify non-small cell lung cancer (NSCLC) patients who may benefit from treatment with the targeted therapy listed in Table 1 in accordance with the approved therapeutic product labeling.

Table 1. Companion Diagnostic Indications

Indication	Biomarker	Therapy
Non-small cell lung cancer (NSCLC)	EGFR Exon 19 deletions, L858R, and T790M*	TAGRISSO® (osimertinib)

A negative result from a plasma specimen does not assure that the patient's tumor is negative for genomic findings. NSCLC patients who are negative for the biomarkers listed in Table 1 should be reflexed to tissue biopsy testing for Table 1 biomarkers using an FDA-approved tumor tissue test, if feasible.

*The efficacy of TAGRISSO® (osimertinib) has not been established in the EGFR T790M plasma-positive, tissue-negative or unknown population and clinical data for T790M plasma-positive patients are limited; therefore, testing using plasma specimens is most appropriate for consideration in patients from whom a tumor biopsy cannot be obtained.

Additionally, the test is intended to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for cancer patients with any solid malignant neoplasm. The test is for use with patients previously diagnosed with cancer and in conjunction with other laboratory and clinical findings.

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

Guardant360 CDx is a single-site assay performed at Guardant Health, Inc.

Warnings and Precautions

- Alterations reported may include somatic (not inherited) or germline (inherited) alterations. The assay filters germline variants from reporting except for pathogenic BRCA1, BRCA2, ATM, and CDK12 alterations. However, if a reported alteration is suspected to be germline, confirmatory testing should be considered in the appropriate clinical context.
- The test is not intended to replace germline testing or to provide information about cancer predisposition.
- Somatic alterations in ATM and CDK12 are not reported by the test as they are excluded from the test's reportable range.
- Genomic findings from cfDNA may originate from circulating tumor DNA (ctDNA) fragments, germline alterations, or non-tumor somatic alterations, such as clonal hematopoiesis of indeterminate potential (CHIP).
- Allow the tube to fill completely until blood stops flowing into the tube. Underfilling of tubes with less than 5 mL of blood (bottom of the label indicates 5 mL fill when tube is held vertically) may lead to incorrect analytical results or poor product performance. This tube has been designed to fill with 10 mL of blood.

Limitations

- For in vitro diagnostic use.
- For prescription use only. This test must be ordered by a qualified medical professional in accordance with clinical laboratory regulations.
- The efficacy of TAGRISSO® (osimertinib) has not been established in the EGFR T790M plasma-positive, tissue-negative or unknown population and clinical data for T790M plasma-positive patients are limited; therefore, testing using plasma specimens is most appropriate for consideration in patients from whom a tumor biopsy cannot be obtained.
- TAGRISSO® efficacy has not been established in patients with EGFR exon 19 deletions < 0.08% MAF, in patients with EGFR L858R < 0.09% MAF, and in patients with EGFR T790M < 0.03% MAF.
- The test is not intended to be used for standalone diagnostic purposes.
- The test is intended to be performed on specific serial number-controlled instruments by Guardant Health, Inc.
- A negative result for any given variant does not preclude the presence of this variant in tumor tissue.
- Decisions on patient care and treatment must be based on the independent medical judgment of the treating physician, taking into consideration all applicable information concerning the patient's condition, such as patient and family history, physical examinations, information from other diagnostic tests, and patient preferences, in accordance with the standard of care.
- ctDNA shedding rate may be lower in patients with primary central nervous system (CNS) tumors.

Definition of Categories

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

Category	Prescriptive use for Therapeutic Product	Clinical Performance	Analytical Performance	Comments
Category 1: Companion Diagnostic (CDx)	Yes	Yes	Yes	ctDNA biomarkers linked to the safe and effective use of the corresponding therapeutic product, for which Guardant360 CDx has demonstrated clinical performance shown to support therapeutic efficacy and strong analytical performance for the biomarker.
Category 2: ctDNA Biomarkers with Strong Evidence of Clinical Significance in ctDNA	No	No	Yes	ctDNA biomarkers with strong evidence of clinical significance presented by other FDA-approved liquid biopsy companion diagnostics for which Guardant360 CDx has demonstrated analytical reliability but not clinical performance.
Category 3A: Biomarkers with Evidence of Clinical Significance in tissue supported by: strong analytical validation using ctDNA	No	No	Yes	ctDNA biomarkers with evidence of clinical significance presented by tissue-based FDA-approved companion diagnostics or professional guidelines for which Guardant360 CDx has demonstrated analytical performance including analytical accuracy, and concordance of blood-based testing to tissue-based testing for the biomarker.
Category 3B: Biomarkers with Evidence of Clinical Significance in tissue supported by: analytical validation using ctDNA	No	No	Yes	ctDNA biomarkers with evidence of clinical significance presented by tissue-based FDA-approved companion diagnostics or professional guidelines for which Guardant360 CDx has demonstrated minimum analytical performance including analytical accuracy.
Category 4: Other Biomarkers with Potential Clinical Significance	No	No	Yes	ctDNA biomarkers with emergent evidence based on peer-reviewed publications for genes/variants in tissue, variant information from well-curated public databases, or in-vitro pre-clinical models, for which Guardant360 CDx has demonstrated minimum analytical performance.

Performance Characteristics

Please refer to product label, www.guardant360cdx.com/technicalinfo. Clinical Performance has not been established for biomarkers in categories 2, 3A, 3B and 4. Guardant360 CDx is indicated to report the following SNVs (AKT1, ALK, APC, AR, ARAF, ATM[#], BRAF, BRCA1^{##}, BRCA2^{##}, CCND1, CDH1, CDK4, CDK6, CDK12[#], CDKN2A, CTNNB1, EGFR, ERBB2, ESR1, FGFR1, FGFR2, FGFR3, GATA3, GNAI1, GNAQ, HRAS, IDH1, IDH2, KIT, KRAS, MAP2K1, MAP2K2, MET, MLH1, MTOR, MYC, NF1, NFE2L2, NRAS, NTRK1, NTRK3, PDGFRA, PIK3CA, PTEN, RAF1, RET, RHEB, ROS1, SMAD4, SMO, STK11, TERT, TSC1, VHL), Indels (ALK, AKT1, APC, ATM[#], BRAF, BRCA1^{##}, BRCA2^{##}, CDH1, CDK12[#], CDKN2A, EGFR, ERBB2, ESR1, FGFR2, GATA3, HNF1A, HRAS, KIT, KRAS, MET, MLH1, NF1, PDGFRA, PIK3CA, PTEN, RET, ROS1, STK11, TSC1, VHL), Fusion (ALK, NTRK1, RET, ROS1), and Amplifications (ERBB2, MET).

[#]Reporting is enabled for pathogenic germline alterations only. Somatic alterations will not be reported. | ^{##}Reporting is enabled for both germline and somatic alterations.

Testing performed at: Guardant Health
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