REPORTING

Report Date:	JUN-30-2018
Receipt Date:	JUN-26-2018
Collection Date:	JUN-25-2018
Specimen:	Blood
Status:	FINAL

PHYSICIAN

Kimberly Schlesinger
Account: Tappahannock Cancer Institute
Address: 618 Hospital Rd, Tappahannock, VA, 22560, United States
Ph: (804) 443-6137 | Fax: (888) 974-3986
Additional Recipient: N/A

Complete Tumor Response Map on page 2

Summary of Somatic Alterations & Associated Treatment Options

KEY ✓ Approved in indication ~ Approved in other indication ✗ Lack of response

Alteration	% cfDNA or Amplification	Associated FDA-approved therapies	Clinical trial availability (see page 3)
TP53 C238R	0.2%	None	Yes

Variants of Uncertain Significance

CDKN2A L32_L37del (0.2%)
The functional consequences and clinical significance of alterations are unknown. Relevance of therapies targeting these alterations is uncertain.

Comments

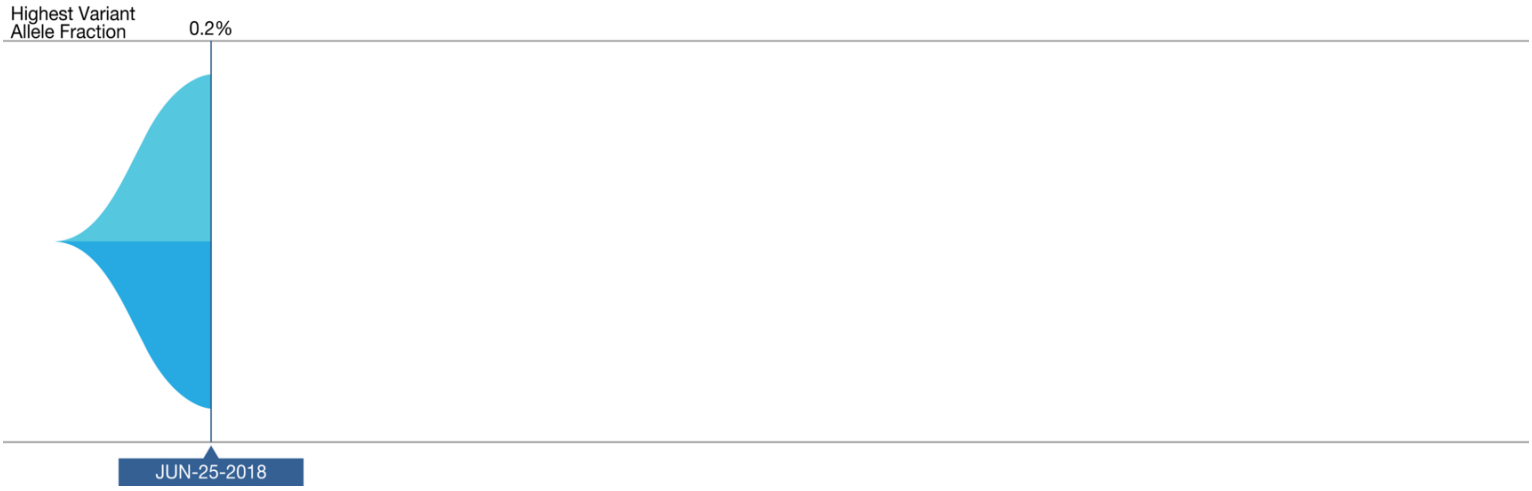
Mircrosatellite status: MSI-High NOT DETECTED

We evaluated 73 genes, including the following guideline-recommended genes for NSCLC:

EGFR (T790M and others)	*ALK*	*ROS1*	*BRAF*	*MET*	*ERBB2* (HER2)	*RET*

Guardant360 Tumor Response Map

The Guardant360 Tumor Response Map illustrates the variant allele fraction (% cfDNA) of observed somatic variants at each sample submission time point. Amplifications are not plotted, and only the first and last five test dates are plotted. Please see the Physician Portal (portal.guardanthealth.com) for the Tumor Response Map with all test dates.



Alteration	% cfDNA or Amp	
TP53 C238R	0.2%	
CDKN2A L32_L37del	0.2%	Variant of Uncertain Significance §

The table above annotates the variant allele fraction (% cfDNA) detected in this sample, listed in descending order.
§ See definitions section for more detail

Available Clinical Trials (within the same state as the ordering physician)

There may be additional trials not listed here. Visit: **portal.guardanthealth.com** or email **clientservices@guardanthealth.com** with A0112848 in the subject line of the email, for additional trials.

Alteration	Trial ID / Contact	Title	Phase	Site(s)
TP53 C238R	Visit portal.guardanthealth.com for trials not within the same state as the physician's office			

More clinical trial options available at **portal.guardanthealth.com**

Definitions

Variant of Uncertain Significance: The functional consequences and clinical significance of alterations are unknown. Relevance of therapies targeting these alterations is uncertain.

Deletion (Del): The following alteration was detected in this patient: CDKN2A L32_L37del. Guardant360 detects short deletions in exons of certain genes (see Table 1), including potential splice site-disrupting events.

Interpretation

Somatic alterations were detected in the circulating cell-free DNA isolated from this patient's blood specimen. These genomic alterations are cancer-associated somatic variants, some of which have been associated with either increased or reduced clinical response to specific treatments. The percentage of altered cell-free DNA circulating (% cfDNA) in blood is related to the unique tumor biology of each patient. Factors that may affect the % cfDNA of detected somatic alterations include tumor growth, turn over, size, heterogeneity, vascularization, disease progression, and treatment.

Method and Limitations

Guardant360 sequences 73 cancer-associated genes to identify somatic alterations. Cell-free DNA (cfDNA) is extracted from plasma, enriched for targeted regions, and sequenced using the Illumina platform and hg19 as the reference genome. All exons are sequenced in some genes; only clinically significant exons are sequenced in other genes. The types of genomic alterations detected by Guardant360 include single nucleotide variants, gene amplifications, fusions, short insertions/deletions, and splice site-disrupting events (see Table 1). Microsatellite Instability (MSI) is assessed for all cancer types by evaluating somatic changes in the length of repetitive sequences on the Guardant360 panel. A “Not Detected” result does not preclude MSI-High status in tissue. MSI status is currently not reported for specimens originating from New York State or for earlier panel versions. This version of the Guardant360 test is not validated for the detection of other types of genomic alterations, such as complex rearrangements or gene deletions. Certain sample or variant characteristics, such as low cfDNA concentration, may result in reduced analytic sensitivity. Guardant360 cannot discern the source of circulating cfDNA, and for some variants in the range of ~40 to 60% cfDNA, the test cannot easily distinguish germline variants from somatic alterations. Guardant360 is not validated for the detection of germline or de novo variants that are associated with hereditary cancer risk. Tissue genotyping should be considered when plasma genotyping is negative, if clinically appropriate.

Table 1: Genes on the Guardant360 Panel

Guardant360 reports single nucleotide variants and splice site mutations in all clinically relevant exons in 73 genes and reports other variant types in select genes as indicated below.

AKT1	*ALK* #	*APC* Ω	*AR* †	*ARAF*	*ARID1A* Ω	*ATM* Ω	*BRAF* †	*BRCA1* Ω
BRCA2 Ω	*CCND1* †	*CCND2* †	*CCNE1* †	*CDH1* Ω	*CDK4* †	*CDK6* †	*CDKN2A* Ω	*CTNNB1*
DDR2	*EGFR* †Ω	*ERBB2* †Ω	*ESR1*	*EZH2*	*FBXW7*	*FGFR1* †	*FGFR2* †#	*FGFR3* #
GATA3 Ω	*GNA11*	*GNAQ*	*GNAS*	*HNF1A*	*HRAS*	*IDH1*	*IDH2*	*JAK2*
JAK3	*KIT* †Ω	*KRAS* †	*MAP2K1*	*MAP2K2*	*MAPK1*	*MAPK3*	*MET* †Ω	*MLH1* Ω
MPL	*MTOR* Ω	*MYC* †	*NF1* Ω	*NFE2L2*	*NOTCH1*	*NPM1*	*NRAS*	*NTRK1* #
NTRK3	*PDGFRA* †Ω	*PIK3CA* †	*PTEN* Ω	*PTPN11*	*RAF1* †	*RB1* Ω	*RET* #	*RHEB*
RHOA	*RIT1*	*ROS1* #	*SMAD4* Ω	*SMO*	*STK11* Ω	*TERT* ‡	*TP53* Ω	*TSC1* Ω
VHL Ω								

Ω Guardant360 reports insertion and deletion variants (indels) in this gene.
‡ Guardant360 reports alterations in the promoter region of this gene.
# Guardant360 reports fusion events involving this gene for all known gene partners.
† Guardant360 reports amplifications of this gene.

About the Test

The Guardant360 assay was developed and its performance characteristics were determined by Guardant Health, Inc. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary. This test may be used for clinical purposes and should not be regarded as investigational or for research only. Guardant Health's clinical reference laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical laboratory testing. The laboratory report should be interpreted in the context of other clinical information and laboratory, pathology, and imaging studies by a qualified medical professional prior to initiating or changing a patient's treatment plan. The selection of any, all, or none of the drugs associated with potential clinical benefit (or potential lack of clinical benefit) is entirely at the discretion of the treating medical professional. Drug and trial information are based on the diagnosis written on the submitted test request form; this information is not based on any supplemental information provided by the requesting medical professional, including pathology reports or other molecular studies. Some drugs listed in this report may not be approved or cleared by the FDA for the indicated use. Guardant Health makes no endorsement, express or implied, of any product, physician, or procedure contained in this report. This report makes no promises or guarantees that a particular medication will affect (or not affect) the clinical outcome of any patient.

Testing performed at: Guardant Health

Laboratory Director: Arthur Baca, MD PhD | CLIA ID: 05D2070300 | CAP #: 8765297 | 505 Penobscot Drive, Redwood City, CA, 94063, United States

Additional information is available

Any therapeutic annotations are based on publicly available information. This information is described in the "Detailed Therapy Results" and "Relevance of Detected Alterations" sections.

Visit portal.guardanthealth.com or email clientservices@guardanthealth.com with A0112848 in the subject line of the email for:

– Additional clinical trials
– Detailed Therapy Results
– Relevance of Detected Alterations
– References

If you would like to receive this additional information with every Guardant360 report, please call client services at 855.698.8887 to opt-in.