REPORTING
Original Report Date: MAY-16-2016
Amended Date: AUG-03-2018
Receipt Date: MAY-04-2016
Collection Date: MAY-03-2016
Specimen: Blood
Status: AMENDED

PHYSICIAN
SQAPortalPhysician O'SQAPortalPhysician
Account: GHSQA Test Account - Please Disregard
Address: 123 GHSQA Test Drive, Suite 2000, Redwood City, CA, 94063, United States
Ph: (650) 123-4567 | Fax: (888) 974-3986
Additional Recipient: N/A

Complete Tumor Response Map on page 2

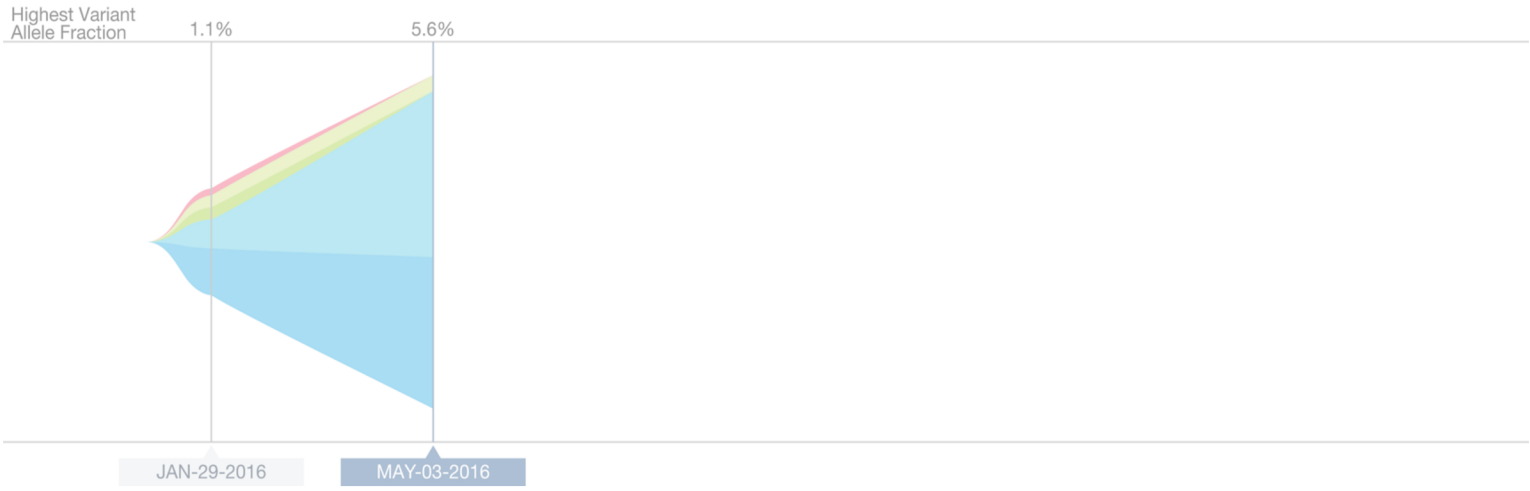
Summary of Somatic Alterations & Associated Treatment Options

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

Alteration	% cfDNA or Amplification	Associated FDA-approved therapies	Clinical trial availability (see page 4)
PIK3CA E542K	5.6%	~ Everolimus, Temsirolimus	Yes
FGFR2 N549K	5.0%	~ Lenvatinib, Nintedanib, Pazopanib, Ponatinib, Regorafenib	Yes
KIT S628N	0.3%	~ Axitinib, Cabozantinib, Dasatinib, Everolimus, Imatinib, Lenvatinib, Nilotinib, Pazopanib, Ponatinib, Regorafenib, Sorafenib, Sunitinib, Temsirolimus	Yes
CCND2 Amplification	Low (+)	None	No
CCNE1 Amplification	Low (+)	None	No
CDK4 Amplification	Low (+)	None	No

Guardant360 Tumor Response Map

The Guardant360 Tumor Response Map illustrates the mutant allele percentage (% 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	Alteration Trend
PIK3CA E542K	5.6%	0.6% → 5.6%
FGFR2 N549K	5.0%	1.1% → 5%
KIT S628N	0.3%	0.2% → 0.3%
CCND2 Amplification Amplifications not graphed above	Low (+)	Plasma copy number
CCNE1 Amplification Amplifications not graphed above	Low (+)	Plasma copy number
CDK4 Amplification Amplifications not graphed above	Low (+)	Plasma copy number
NF1 R440*	ND	0.2% → ND

Alteration	% cfDNA or Amp	Alteration Trend
ERBB2 (HER2) R849W	ND	

The table above annotates the variant allele fraction (% cfDNA) detected in this sample, listed in descending order.

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 A27433 in the subject line of the email, for additional trials.

Alteration	Trial ID / Contact	Title	Phase	Site(s)
PIK3CA E542K	NCT01674140			San Jose, California (2) Rancho Mirage, California Palo Alto, California (2) Loma Linda, California Additional trial sites available
	NCT01633060			Los Angeles, California (2) Fountain Valley, California Monterey, California
FGFR2 N549K	NCT01703481			Los Angeles, California Sacramento, California La Jolla, California
	NCT01466972			San Francisco, California
KIT S628N	NCT02049957			San Francisco, California Santa Barbara, California Los Angeles, California
	NCT02258451			La Jolla, California Long Beach, California Bakersfield, California San Francisco, California Los Angeles, California

More clinical trial options available at portal.guardanthealth.com

Definitions

Somatic Alterations Not Detected (ND): Somatic alterations may be present that are below the limit of detection of this test. Certain sample or variant characteristics may result in reduced analytic sensitivity. The absence of detectable somatic alterations in circulating cell-free DNA does not preclude the presence of somatic alterations in the tumor.

Amplification: Guardant360 detects amplifications in the genes listed in Table 1. Gene amplification results in increased copies of the gene present in the cfDNA. The reported absolute copy number value represents the average copy number for the detected gene that was detected in circulating cfDNA. With the exception of sex-linked genes such as AR, 2 copies are expected in the absence of amplification. As the absolute number of copies in circulation is dependent on both tumor fraction and the magnitude of the tumor amplification, amplifications are reported on a semi-quantitative scale:

Low (+): Amplification magnitude is below the 50th percentile of amplifications detected by Guardant360.
Medium (++): Amplification magnitude is between the 50th and 90th percentiles.
High (+++): Amplification magnitude is above the 90th percentile.

Comments

None

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.

Amplification was detected in the circulating cell-free DNA isolated from this patient’s blood specimen for the annotated gene(s). Unlike tissue-based gene amplification tests (e.g. IHC or FISH), Guardant360 assesses the total representation of a given gene in all circulating cell-free DNA present in the patient’s blood sample including material derived from the tumor and healthy tissue alike. As such, the absolute level of amplification present in the blood depends both on the tumor-derived cfDNA content and on the degree of amplification within that fraction and cannot be inferred from bulk cfDNA interrogation. For example, a positive Guardant360 test could represent a small population of cells with extremely high levels of the detected gene amplification. Alternatively, it could represent a large population of cells with low to medium levels of the detected gene amplifications. The exact correlation between amplification detected by Guardant360 compared to IHC or FISH and how each test differentially guides patient management is an area of active investigation.

Method and Limitations

Guardant360 sequences 73 cancer-associated genes to identify somatic alterations with high sensitivity. Cell-free DNA is extracted from plasma, and genomic alterations are analyzed by massively parallel sequencing of amplified target genes using the Illumina sequencing platforms 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 variations, amplifications, fusions, short insertions/deletions, and splice site-disrupting events (see Table 1). 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 may result in reduced analytic sensitivity, such as low cell-free DNA concentration. Guardant360 cannot discern the source of the 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*	*AR* †	*ARAF*	*ARID1A*	*ATM*	*BRAF* †	*BRCA1*
BRCA2	*CCND1*	*CCND2*	*CCNE1* †	*CDH1*	*CDK4* †	*CDK6* †	*CDKN2A*	*CDKN2B*
CTNNB1	*EGFR* †	*ERBB2* †	*ESR1*	*EZH2*	*FBXW7*	*FGFR1* †	*FGFR2* †#	*FGFR3* #
GATA3	*GNA11*	*GNAQ*	*GNAS*	*HNF1A*	*HRAS*	*IDH1*	*IDH2*	*JAK2*
JAK3	*KIT* †	*KRAS* †	*MAP2K1*	*MAP2K2*	*MET* †	*MLH1*	*MPL*	*MYC* †
NF1	*NFE2L2*	*NOTCH1*	*NPM1*	*NRAS*	*NTRK1* #	*PDGFRA* †	*PIK3CA* †	*PTEN*
PTPN11	*RAF1* †	*RB1*	*RET* #	*RHEB*	*RHOA*	*RIT1*	*ROS1* #	*SMAD4*
SMO	*SRC*	*STK11*	*TERT*	*TP53*	*TSC1*	*VHL*		

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

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 considered in context with other clinical criteria (e.g. patient history, physical exam), as well as 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. Drugs and trial information are based on the diagnosis as 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 a particular 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 A27433 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.