ABOUT GUARDANT360

Guardant360 detects cell-free circulating tumor DNA (ctDNA) in blood specimens of advanced solid-tumor cancer patients and evaluates 73 genes. It tests four major classes of alterations relevant for treatment selection: point mutations, indels (insertions/deletions), copy number amplifications, and fusions/rearrangements.

Guardant Health's proprietary Digital Sequencing method optimizes next generation sequencing for accurate tumor variant detection at the low allele fractions present in cell-free DNA. High-efficiency capture enables single molecule detection, optimizing sensitivity, while unique digital barcoding and custom bioinformatics analysis optimizes specificity.[1]

INDICATIONS FOR USE TO GUIDE TREATMENT DECISIONS

Before first-line therapy

- When molecular testing is incomplete, limited, or unobtainable
- For example, when a patient is *EGFR* and *ALK* negative but lacks sufficient tissue for *ROS1* or *BRAF* testing

At progression

- To avoid an invasive biopsy when looking for a new genomic target
- For patients whose tissue testing was incomplete at initial diagnosis

Not indicated for:

- Hematologic malignancies
- Early stage (stage I/II) cancers
- When disease is stable or responding to therapy

TEST SPECIFICATIONS

Sample type and volume

Two 10 mL tubes of whole blood.

Storage and shipping conditions

Do not freeze or refrigerate. Ship same or next day at room temperature.

Test turnaround time

7 calendar days from sample receipt to results.

PERFORMANCE SPECIFICATIONS

Alteration Type	Reportable Range	Allelic Fraction/ Copy Number	Analytical Sensitivity	Analytical Specificity*
SNVs	≥0.04%	>0.25%	100%	97%
		0.05-0.25%	64%	
Indels	≥0.02%	>0.20%	100%	100%
		0.05-0.20%	68%	
Fusions	≥0.04%	>0.20%	95%	100%
		0.05-0.20%	83%	
CNAs	≥2.12 copies	2.24 copies**	95%	100%

Based on cell-free DNA input of 30 ng in patient samples. Analytical sensitivity cited above are for targeted, clinically important regions. Sensitivity outside these regions or in highly repetitive sequence contexts may vary.

* Per sample, over entire genomic reportable range of Guardant360 panel.

** Equivalent to 5% tumor fraction and 8 *ERBB2* (HER2) gene copies in tumor. Copy number sensitivity may vary with other genes (2.24 - 2.76 copies).

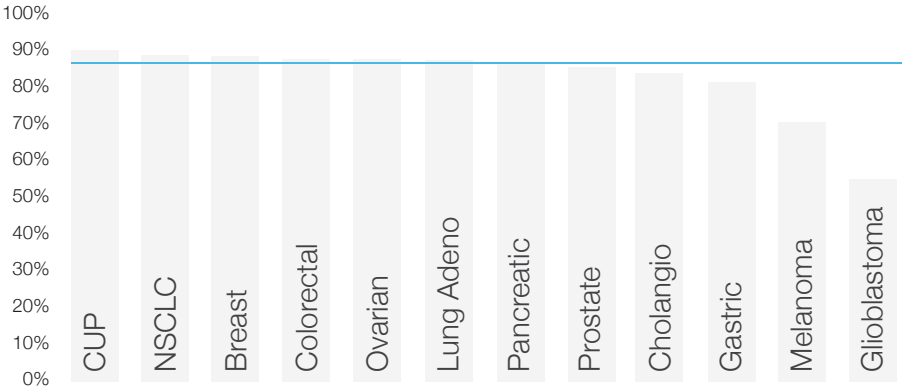
INCLUDES ALL GUIDELINE-RECOMMENDED GENES FOR SOLID-TUMOR CANCERS

CRITICAL OR ALL EXONS* COMPLETELY SEQUENCED AND ALL FOUR MAJOR CLASSES OF ALTERATIONS

Point Mutations (SNVs) *(73 Genes)*						Indels *(23 Genes)*		Amplifications *(18 Genes)*		Fusions *(6 Genes)*
AKT1	***ALK***	*APC*	*AR*	*ARAF*	*ARID1A*	*ATM*	*APC*	*AR*	*BRAF*	***ALK***
ATM	***BRAF***	*BRCA1*	*BRCA2*	*CCND1*	*CCND2*	*ARID1A*	*BRCA1*	*CCND1*	*CCND2*	*FGFR2*
CCNE1	*CDH1*	*CDK4*	*CDK6*	*CDKN2A*	*CTNNB1*	*BRCA2*	*CDH1*	*CCNE1*	*CDK4*	*FGFR3*
DDR2	***EGFR***	***ERBB2 (HER2)***	*ESR1*	*EZH2*	*FBXW7*	*CDKN2A*	***EGFR***	*CDK6*	*EGFR*	*NTRK1*
FGFR1	*FGFR2*	*FGFR3*	*GATA3*	*GNA11*	*GNAQ*	***ERBB2***	*GATA3*	*ERBB2*	*FGFR1*	***RET***
GNAS	*HNF1A*	*HRAS*	*IDH1*	*IDH2*	*JAK2*	*KIT*	***MET***	*FGFR2*	*KIT*	***ROS1***
JAK3	*KIT*	*KRAS*	*MAP2K1/MEK1*	*MAP2K2/MEK2*	*MAPK1/ERK2*	*MLH1*	*MTOR*	*KRAS*	***MET***	
MAPK3/ERK1	***MET***	*MLH1*	*MPL*	*MTOR*	*MYC*	*NF1*	*PDGFRA*	*MYC*	*PDGFRA*	
NF1	*NFE2L2*	*NOTCH1*	*NPM1*	*NRAS*	*NTRK1*	*PTEN*	*RB1*	*PIK3CA*	*RAF1*	
NTRK3	*PDGFRA*	*PIK3CA*	*PTEN*	*PTPN11*	*RAF1*	*SMAD4*	*STK11*			
RB1	***RET***	*RHEB*	*RHOA*	*RIT1*	***ROS1***	*TP53*	*TSC1*			
SMAD4	*SMO*	*STK11*	*TERT*†	*TP53*	*SC1*	*VHL*				
VHL										

NSCLC guideline-recommended genes shown in bold / *Exons selected to maximize detection of known somatic mutations / † Includes *TERT* promoter region

ctDNA DETECTION RATE BY CANCER TYPE WITH THE GUARDANT360 ASSAY



Average across cancer types: 86%

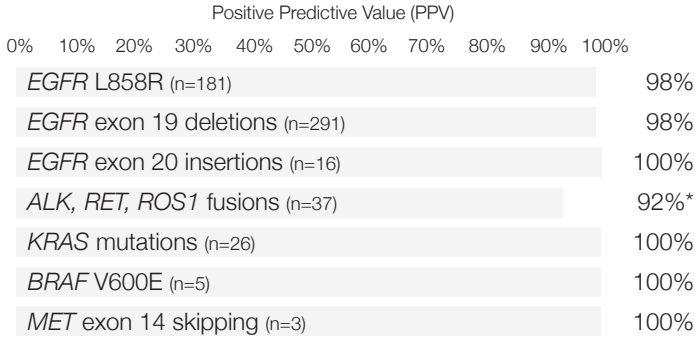
Tumors stabilized by therapy typically do not shed as much DNA into circulation, nor do tumors that are slow-growing.[2] In these clinical contexts, Guardant360 may not detect any tumor DNA in a patient sample.

Based on 24,000 consecutive clinical samples

COMPARISON OF PAIRED TISSUE AND GUARDANT360 RESULTS

92-100%

of Guardant360-detected NSCLC driver alterations were also found in tissue (positive predictive value)[3]



*3 of 3 Guardant360 *ALK*-fusion positive, tissue-negative (by FISH) cases were treated with and responded to crizotinib, suggesting tissue false-negatives.[4]

REFERENCES: 1. Lanman et al. PloS One 2015 / 2. Holdenrieder et al. Clin Cancer Res 2004; Bettegowda, et al. Sci Transl Med 2014 / 3. Mack et al. J Thorac Oncol Suppl 2016 / 4. McCoach et al. Under Review 2018

GUARDANT HEALTH