Jones, Lewis (A0123456)
Patient MRN: - | DOB: FEB-01-1956 | Gender: Male
Diagnosis: Prostate adenocarcinoma | Test Number 1

GUARDANT360
Therapy Finder Page

REPORTING

Report Date:	DEC-29-2020
Receipt Date:	DEC-23-2020
Collection Date:	DEC-22-2020
Specimen:	Blood
Status:	FINAL

PHYSICIAN
John Miller

Account: Pleasantville Oncology
Address: 1234 Main Street
Anaheim, CA 94063, United States Ph: (123) 456-7890 | Fax: (123) 456
Additional Recipient: N/A

Complete Tumor Response Map on page 3

Summary of Detected Somatic Alterations, Immunotherapy Biomarkers & Associated Treatment Options

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

Detected Alteration(s) / Biomarker(s)	Associated FDA-approved therapies	Clinical trial availability (see page 5)	% cfDNA or Amplification
AR H875Y	✓ **Bicalutamide, Degarelix, Flutamide, Goserelin, Leuprolide, Nilutamide, Triptorelin** ✗ **Abiraterone, Apalutamide, Enzalutamide**	Yes	0.5%
CHEK2 R346H	✓ **Olaparib** ~ Niraparib, Rucaparib, Talazoparib	Yes	1.8%
BRCA2 I605fs	✓ **Olaparib, Rucaparib** ~ Niraparib, Talazoparib	Yes	2.3%
MSI-High	✓ **Pembrolizumab** ~ Atezolizumab, Avelumab, Durvalumab, Nivolumab	Yes	DETECTED

Variants of Uncertain Significance
NTRK2 A31T (3.5%), *BRAF* A762V (2.2%), *PALB2* R37C (1.9%), *DDR2* P157L (0.3%), *GNA11* G208fs (0.3%)
The functional consequences and clinical significance of alterations are unknown. Relevance of therapies targeting these alterations is uncertain.

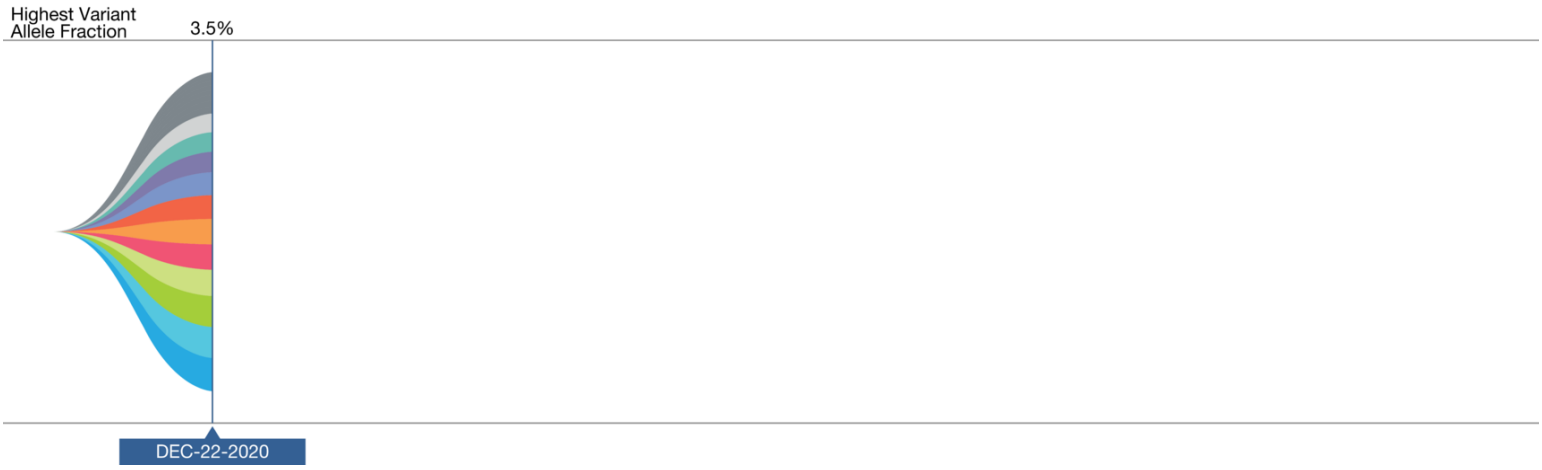
Synonymous Alterations
CTNNB1 R550R (3.2%), *NTRK1* T741T (1.7%), *MPL* P530P (0.3%), *ALK* Y1584Y (0.2%), *ARID1A* P1710P (0.1%)
This sequence change does not alter the amino acid at this position and is unlikely to be a therapeutic target. Clinical correlation is advised.

Additional Biomarkers

Biomarker	Additional Details
Tumor Mutational Burden (TMB)	81.47 mut/MB
MSI-High	DETECTED

Guardant360 Tumor Response Map

The Guardant360 Tumor Response Map illustrates the variant allele fraction (% cfDNA) of observed somatic variants at each sample submission. 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.



Detected Alteration(s) / Biomarker(s)	% cfDNA or Amp	
NTRK2 A31T	3.5%	Variant of Uncertain Significance §
PTEN E157fs	3.2%	
CTNNB1 R550R	3.2%	Synonymous Alteration §
PIK3CA E545K	2.6%	
PTEN K267fs	2.5%	
FANCA R1400H	2.5%	
BRCA2 I605fs	2.3%	
BRAF A762V	2.2%	Variant of Uncertain Significance §
PALB2 R37C	1.9%	Variant of Uncertain Significance §
CHEK2 R346H	1.8%	

Detected Alteration(s) / Biomarker(s)	% cfDNA or Amp	
NTRK1 T741T	1.7%	Synonymous Alteration §
AR H875Y	0.5%	
NOTCH1 F357del	0.4%	
MTOR W1456R	0.4%	
GNA11 G208fs	0.3%	Variant of Uncertain Significance §
DDR2 P157L	0.3%	Variant of Uncertain Significance §
MPL P530P	0.3%	Synonymous Alteration §
NOTCH1 S2486fs	0.2%	
ALK Y1584Y	0.2%	Synonymous Alteration §
ARID1A P1710P	0.1%	Synonymous Alteration §

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 A0315341 in the subject line of the email, for additional trials.

Alteration	Trial ID / Contact	Title	Phase	Site(s)
MSI-High	NCT03170960 Exelixis Clinical Trials,druginfo@exelixis.com,1-888-EXELIXIS (888-393-5494)	Study of Cabozantinib in Combination With Atezolizumab to Subjects With Locally Advanced or Metastatic Solid Tumors	Phase 1 /Phase 2	Lexington, KY
	NCT03767348 Clinical Trials at Replimune, Clinicaltrials@replimune.com,1-781-222-9570	Study of RP1 Monotherapy and RP1 in Combination With Nivolumab	Phase 2	Louisville, KY
	NCT03836352 See https://clinicaltrials.gov/show/NCT03836352	Study of an Immunotherapeutic, DPX-Survivac, in Combination With Low Dose Cyclophosphamide & Pembrolizumab, in Subjects With Selected Advanced & Recurrent Solid Tumors	Phase 2	Louisville, KY
	NCT04100018 Recruiting sites have contact information. Please contact the sites directly. If there is no contact information,,Clinical.Trials@bms.com,please email:	A Study of Nivolumab or Placebo in Combination With Docetaxel in Men With Advanced Castration-resistant Prostate Cancer	Phase 3	Louisville, KY
	NCT04123366 Toll Free Number,Trialsites@merck.com,1-888-577-8839	Study of Olaparib (MK-7339) in Combination With Pembrolizumab (MK-3475) in the Treatment of Homologous Recombination Repair Mutation (HRRm) and/or Homologous Recombination Deficiency (HRD)-Positive Advanced Cancer (MK-7339-007/KEYLYNK-007)	Phase 2	Louisville, KY
	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
BRCA2 I605fs	NCT03742895 Toll Free Number,Trialsites@merck.com, 1-888-577-8839	Efficacy and Safety of Olaparib (MK-7339) in Participants With Previously Treated, Homologous Recombination Repair Mutation (HRRm) or Homologous Recombination Deficiency (HRD) Positive Advanced Cancer (MK-7339-002 / LYNK-002)	Phase 2	Lexington, KY
	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
PTEN E157fs	NCT02465060 See https://clinicaltrials.gov/show/NCT02465060	Targeted Therapy Directed by Genetic Testing in Treating Patients With Advanced Refractory Solid Tumors, Lymphomas, or Multiple Myeloma (The MATCH Screening Trial)	Phase 2	Madisonville, KY Paducah, KY Bardstown, KY Louisville, KY (5) Additional trial sites available
	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
AR H875Y	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
CHEK2 R346H	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
PIK3CA E545K	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
FANCA R1400H	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
MTOR W1456R	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			
PTEN K267fs	Visit **portal.guardanthealth.com** for trials not within the same state as the physician's office			

Alteration	Trial ID / Contact	Title	Phase	Site(s)
NOTCH1 F357del	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.

Synonymous Alteration: This sequence change does not alter the amino acid at this position and is unlikely to be a therapeutic target. Clinical correlation is advised.

Insertion (Ins): The following alteration was detected in this patient: *PTEN* E157fs. Guardant360 detects short insertions in exons of certain genes (see Table 1).

Deletion (Del): The following alteration was detected in this patient: *BRCA2* I605fs; *GNA11* G208fs; *NOTCH1* F357del, S2486fs; *PTEN* K267fs. 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 83 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 (SNVs), gene amplifications, fusions, short insertions/deletions (indels, longest detected, 70 base pairs), 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 in samples where the highest % cfDNA is < 0.2% is an inconclusive result because it does not preclude MSI-High status in tissue. Tumor mutational burden (TMB) score is calculated for all cancer types from somatic SNVs and indels in exons of ~ 500 genes detected in cfDNA, followed by adjusting for tumor shedding levels and the size of the panel. A "Not Evaluable" result is an inconclusive result in samples where the evidence of tumor shedding is insufficient and it does not preclude TMB-High status in tissue. 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, splice site mutations, and insertion and deletion variants (indels) in all clinically relevant exons in 83 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*	*CDK12*	*CDK4* †	*CDK6* †	*CDKN2A*
CHEK2	*CTNNB1*	*DDR2*	*EGFR* † #	*ERBB2* †	*ESR1* †	*EZH2*	*FANCA*	*FBXW7*
FGFR1 † #	*FGFR2* †	*FGFR3* #	*GATA3*	*GNA11*	*GNAQ*	*GNAS*	*HNF1A*	*HRAS*
IDH1	*IDH2*	*JAK2*	*JAK3*	*KEAP1*	*KIT* †	*KRAS* †	*MAP2K1*	*MAP2K2*
MAPK1	*MAPK3*	*MET* † #	*MLH1*	*MPL*	*MSH2*	*MSH6*	*MTOR*	*MYC* †
NF1	*NFE2L2*	*NOTCH1*	*NPM1*	*NRAS*	*NTRK1* #	*NTRK2* #	*NTRK3* #	*PALB2*
PDGFRA †	*PIK3CA* †	*PMS2*	*PTEN*	*PTPN11*	*RAD51D*	*RAF1* †	*RB1*	*RET* #
RHEB	*RHOA*	*RIT1*	*ROS1* #	*SMAD4*	*SMO*	*STK11*	*TERT* ‡	*TP53*
TSC1	*VHL*							

‡ Guardant360 reports alterations in the promoter region of this gene.

Guardant360 reports fusion events involving this gene.

† 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: Martina Lefterova, MD PhD | CLIA ID: 05D2070300 | CAP #: 8765297 | 505 Penobscot Drive, Redwood City, CA, 94063, USA

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 A0315341 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.