STUDY

Partner Name Clovis Oncology
Partner Study ID CO-338-063 FACT CF3
FMI Study ID ACT-BPA-PRO-17-685

TEST

FMI Test Order # ORD-0900636-01
Test Type FoundationOne Liquid
Report Date 25 Sep 2020

PATIENT

Subject ID 63-28043-021
Site ID 28043
Sex Male
Date of Birth 01JAN1953
Diagnosis Prostate acinar adenocarcinoma
Physician Name Not Provided

SPECIMEN

Specimen ID 11108967-B31
Sample Type Peripheral Blood
Site Blood
Collection Date 10SEP2020
Received Date 14SEP2020
Visit Type Pre-Screening

ABOUT THE TEST

FoundationOne® Liquid is a next generation sequencing (NGS) assay that identifies clinically relevant genomic alterations in circulating tumor DNA.

GENOMIC FINDINGS

NOTE: This is a comprehensive list of cancer-related alterations detected in this patient's sample.

GENE	ALTERATION
TP53	splice site 559+1G>A

GENOMIC SIGNATURES

NOTE: This section includes information for genomic signatures reported in this test.

Biomarker	Result
Microsatellite Instability Status	Not Evaluable

VARIANTS OF UNKNOWN SIGNIFICANCE

Note: These variants may not have been adequately characterized in the scientific literature at the time this report was issued, and/or the genomic context of these alterations makes significance unclear. FMI VUS are included here, in the event that they become clinically meaningful in the future.

GENE	ALTERATION
PIK3CA	N114D
CDH1	G877R
VEGFA	S129R

APPENDIX

Gene List

FoundationOne® Liquid interrogates the complete exonic sequence of 35 genes, introns of 7 genes involved in rearrangements, and select exons of an additional 35 genes. The assay will be updated periodically to reflect new knowledge about cancer biology.

DNA GENE LIST: ENTIRE CODING SEQUENCE FOR DETECTION OF BASE SUBSTITUTIONS, INSERTION/DELETIONS, AND COPY NUMBER ALTERATIONS

APC	*AR*	*ATM*	*BRCA1*	*BRCA2*	*CCND1*	*CD274 (PD-I1)*	*CDH1*	*CDK4*
CDK6	*CDK12*	*CDKN2A*	*CHEK2*	*CRKL*	*EGFR*	*ERBB2*	*ERRFI1*	*FGFR1*
FGFR2	*FOXL2*	*KRAS*	*MDM2*	*MET*	*MYC*	*MYCN*	*NF1*	*PALB2*
PDCD1LG2 (PD-L2)	*PTEN*	*PTPN11*	*RB1*	*SMO*	*STK11*	*TP53*	*VEGFA*	

DNA GENE LIST: SELECT EXONIC SEQUENCE OF THE DETECTION OF BASE SUBSTITUTIONS, INSERTIONS/DELETIONS, AND COPY NUMBER ALTERATIONS

ABL1 Exons 4-9	*AKT1 Exon 3*	*ALK Exons 20-29*	*ARAF Exons 4, 5, 7, 11, 13, 15, 16*	*BRAF Exons 11-18*	*BTK Exons 2, 15*	*CTNNB1 Exon 3*	*DDR2 Exons 5, 17, 18*	*ESR1 Exons 4-8*
EZH2 Exons 4, 16, 18	*FGFR3 Exons 7, 9, 14*	*FLT3 Exons 14, 15, 20*	*GNA11 Exons 4, 5*	*GNAQ Exons 4, 5*	*GNAS Exons 1, 8*	*HRAS Exons 2, 3*	*IDH1 Exon 4*	*IDH2 Exon 4*
JAK2 Exon 14	*JAK3 Exons 5, 11-13, 15, 16*	*KIT Exons 8, 9, 11-13, 17*	*MAP2K1 (MEK1) Exons 2, 3*	*MAP2K2 (MEK2) Exons 2-4, 6, 7*	*MPL Exon 10*	*MTOR Exons 19, 30, 39, 40, 43-45, 47, 48, 53, 56*	*MYD88 Exon 4*	*NPM1 Exons 4-6, 8, 10*
NRAS Exons 2, 3	*PDGFRA Exons 12, 18*	*PDGFRB Exons 12-21, 23*	*PIK3CA Exons 2, 3, 5-8, 10, 14, 19, 21 (Coding Exons 1, 2, 4-7, 9, 13, 18, 20)*	*RAF1 Exons 3-7, 10, 14, 15, 17*	*RET Exons 11, 13-16*	*ROS1 Exons 36-38, 40*	*TERT (Promoter only)*	

DNA GENE LIST: FOR THE DETECTION OF SELECT REARRANGEMENTS

ALK	*EGFR*	*FGFR2*	*FGFR3*	*PDGFRA*	*RET*	*ROS1*

ADDITIONAL GENOMIC SIGNATURES
Microsatellite Status (MS)

Performance Specifications

PERFORMANCE SPECIFICATIONS			
	Mutant Allele Frequency (MAF)/ Tumor Fraction[1]	**Sensitivity**[2]	**Positive Predictive Value**(PPV)[2]
Base substitutions	> 0.5%	100% (CI 99.7% - 100%)	100% (CI 99.7% - 100%)
	0.25% - 0.5%	96.4% (CI 94.3% - 97.8%)	100% (CI 99.0% - 100%)
	0.125% - 0.25%	62.6% (CI 58.2% - 66.7%)	99.7% (CI 98% - 100%)
Insertions/Deletions (Indels) (1-40bp)	> 0.5%	99.7% (CI 98.8% - 99.9%)	100% (CI 99.3% - 100%)
	0.25% - 0.5%	92.1% (CI 87% - 95.3%)	100% (CI 97.3.0% - 100%)
	0.125% - 0.25%	61.4% (CI 54% - 68.3%)	100% (CI 96% - 100%)
Rearrangements[3]	> 0.5%	100% (CI 90.2% - 100%)	100% (CI 90.2% - 100%)
	0.25% - 0.5%	100% (CI 74.7% - 100%)	100% (CI 74.7% - 100%)
	0.125% - 0.25%	86.7% (CI 58.4% - 97.7%)	100% (CI 71.7% - 100%)
Copy Number Amplifications (CNA)[4]	≥ 20%	95.3% (CI 82.9% - 99.2%)	97.6% (CI 85.9% - 99.9%)
	< 20%	Varies depending on amplitude of CNA and ctDNA fraction	
Microsatellite Instabillity (MSI)[5]	> 2.0%	96.0% (CI 77.7% - 100%)	100% (CI 82.6% - 100%)
	1.0% - 2.0%	69.2% (CI 38.9% - 89.6%)	100% (CI 62.7% - 100%)
Reproducibillity (average concordance between replicates)		97.7% inter-batch precision 95.9% intra-batch precision	
Specimen Type		Peripheral whole blood (see Specimen Instructions for details)	
Turnaround Time[6]		< 2 Weeks	

1. Copy number amplifications were calculated using tumor fraction. **2.** 95% confidence interval. **3.** Performance for gene fusions within targeted introns only. Sensitivity for gene fusions occurring outside targeted introns or in highly repetitive intronic contexts is reduced. **4.** Copy number = 8. **5.** Reported when MSI is determined to be high. **6.** Based on typical turnaround time from receipt of sample

Microsatellite status, which is a measure of microsatellite instability (MSI), is determined by assessing indel characteristics at a subset of homopolymer repeat loci covered by the assay. Microsatellite status is assayed for all FoundationOne Liquid samples and will only be reported if MSI-High is determined.

Assay specifications are based on samples meeting a minimum coverage threshold (>85% if targeted regions must have >2500x redundant coverage). Specimens with higher input mass typically obtain higher coverage and have higher sensitivity for low-frequency alterations.

Certain sample or variant characteristics may result in reduced sensitivity. These include: low sample quality, deletions and insertions >40bp, or repetitive/high homology sequences. FoundationOne Liquid is performed using cell-free DNA, and as such germline events may not be reported. The following targets typically have low coverage resulting in a reduction in sensitivity: TP53 exon 1 and PDGFRA exon 12.

About FoundationOne Liquid

FoundationOne® Liquid was developed and its performance characteristics determined by Foundation Medicine, Inc. (FMI). FoundationOne Liquid is a next generation sequencing (NGS) assay that identifies clinically relevant genomic alterations in circulating tumor DNA. FoundationOne Liquid has not been cleared or approved by the United States Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary. FoundationOne Liquid may be used for clinical purposes and should not be regarded as purely investigational or for research only. Foundation Medicine's clinical reference laboratory is certified under the Clinical Laboratory Improved Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing.

Qualified Alteration Calls (Equivocal)

All equivocal calls, regardless of alteration type, imply that there is adequate evidence to call the alteration with confidence. However, the repeatability of equivocal calls may be lower than non-equivocal calls. The threshold used in FoundationOne Liquid for identifying a copy number amplification is five (5) for ERBB2 and six (6) for all other genes. For copy number amplifications, the equivocal status may be applied to calls in samples with calculated tumor fraction <30% but above the noise threshold. In addition, copy number amplifications in genes with three (3) baited exons are also marked as equivocal.

Treatment Decisions are the Responsibility of Physician.

The information in this Report must be considered in conjunction with all other relevant information regarding a particular patient, before the patient's treating physician recommends a course of treatment. Decisions on patient care and treatment must be based on the independent medical judgement 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 in a given community. A treating physician's decisions should not be based on a single test, such as this Test, or the information contained in this Report.