## STUDY

Partner Name Clovis Oncology
Partner Study ID CO-338-063
FMI Study ID F1S-BPA-PRO-16-468

## TEST

FMI Test Order # ORD-0957975-01
Test Type FoundationOne
Report Date 04 Dec 2020

## PATIENT

Subject ID 63-28043-022
Site ID 28043
Sex Male
Date of Birth 1955
Diagnosis Prostate acinar adenocarcinoma
Physician Name Not Provided

## SPECIMEN

Specimen ID 11103033-A33
Sample Type Slide Deck
Site Prostate
Collection Date 14JUL2020
Received Date 21NOV2020
Visit Type Pre-Screening

**About the Test**

FoundationOne is a next-generation sequencing (NGS) based assay that identifies genomic alterations within hundreds of cancer-related genes.

## GENOMIC FINDINGS

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

| GENE | ALTERATION |
|---|---|
| MYC | amplification - equivocal |
| PTEN | loss |
| TERC | amplification - equivocal |
| TMPRSS2 | TMPRSS2-ERG fusion |
| TP53 | C242F |
| SLIT2 | Y1312fs*4 |

## GENOMIC SIGNATURES

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

| Biomarker | Result |
|---|---|
| Tumor Mutational Burden | 0.88 mutations-per-megabase |
| Microsatellite Instability | MS-Stable |

## 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 |
|---|---|
| NBN | amplification |
| RUNX1T1 | amplification |
| JUN | E166K |
| KRAS | G179S |
| FANCI | Q625* |

APPENDIX

## Gene List

FoundationOne® is designed to include genes known to be somatically altered in human solid tumors and validated targets for therapy, either approved or in clinical trials, and/or unambiguous drivers of oncogenesis based on current knowledge. The current assay interrogates 315 genes as well as introns of 28 genes involved in rearrangements. 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**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *ABL1* | *ABL2* | *ACVR1B* | *AKT1* | *AKT2* | *AKT3* | *ALK* | *AMER1 (FAM123B)* | *APC* | *AR* |
| *ARAF* | *ARFRP1* | *ARID1A* | *ARID1B* | *ARID2* | *ASXL1* | *ATM* | *ATR* | *ATRX* | *AURKA* |
| *AURKB* | *AXIN1* | *AXL* | *BAP1* | *BARD1* | *BCL2* | *BCL2L1* | *BCL2L2* | *BCL6* | *BCOR* |
| *BCORL1* | *BLM* | *BRAF* | *BRCA1* | *BRCA2* | *BRD4* | *BRIP1* | *BTG1* | *BTK* | *C11orf30 (EMSY)* |
| *CARD11* | *CBFB* | *CBL* | *CCND1* | *CCND2* | *CCND3* | *CCNE1* | *CD274* | *CD79A* | *CD79B* |
| *CDC73* | *CDH1* | *CDK12* | *CDK4* | *CDK6* | *CDK8* | *CDKN1A* | *CDKN1B* | *CDKN2A* | *CDKN2B* |
| *CDKN2C* | *CEBPA* | *CHD2* | *CHD4* | *CHEK1* | *CHEK2* | *CIC* | *CREBBP* | *CRKL* | *CRLF2* |
| *CSF1R* | *CTCF* | *CTNNA1* | *CTNNB1* | *CUL3* | *CYLD* | *DAXX* | *DDR2* | *DICER1* | *DNMT3A* |
| *DOT1L* | *EGFR* | *EP300* | *EPHA3* | *EPHA5* | *EPHA7* | *EPHB1* | *ERBB2* | *ERBB3* | *ERBB4* |
| *ERG* | *ERRFI1* | *ESR1* | *EZH2* | *FAM46C* | *FANCA* | *FANCC* | *FANCD2* | *FANCE* | *FANCF* |
| *FANCG* | *FANCL* | *FAS* | *FAT1* | *FBXW7* | *FGF10* | *FGF14* | *FGF19* | *FGF23* | *FGF3* |
| *FGF4* | *FGF6* | *FGFR1* | *FGFR2* | *FGFR3* | *FGFR4* | *FH* | *FLCN* | *FLT1* | *FLT3* |
| *FLT4* | *FOXL2* | *FOXP1* | *FRS2* | *FUBP1* | *GABRA6* | *GATA1* | *GATA2* | *GATA3* | *GATA4* |
| *GATA6* | *GID4 (C17orf39)* | *GLI1* | *GNA11* | *GNA13* | *GNAQ* | *GNAS* | *GPR124* | *GRIN2A* | *GRM3* |
| *GSK3B* | *H3F3A* | *HGF* | *HNF1A* | *HRAS* | *HSD3B1* | *HSP90AA1* | *IDH1* | *IDH2* | *IGF1R* |
| *IGF2* | *IKBKE* | *IKZF1* | *IL7R* | *INHBA* | *INPP4B* | *IRF2* | *IRF4* | *IRS2* | *JAK1* |
| *JAK2* | *JAK3* | *JUN* | *KAT6A (MYST3)* | *KDM5A* | *KDM5C* | *KDM6A* | *KDR* | *KEAP1* | *KEL* |
| *KIT* | *KLHL6* | *KMT2A (MLL)* | *KMT2C (MLL3)* | *KMT2D (MLL2)* | *KRAS* | *LMO1* | *LRP1B* | *LYN* | *LZTR1* |
| *MAGI2* | *MAP2K1* | *MAP2K2* | *MAP2K4* | *MAP3K1* | *MCL1* | *MDM2* | *MDM4* | *MED12* | *MEF2B* |
| *MEN1* | *MET* | *MITF* | *MLH1* | *MPL* | *MRE11A* | *MSH2* | *MSH6* | *MTOR* | *MUTYH* |
| *MYC* | *MYCL (MYCL1)* | *MYCN* | *MYD88* | *NF1* | *NF2* | *NFE2L2* | *NFKBIA* | *NKX2-1* | *NOTCH1* |
| *NOTCH2* | *NOTCH3* | *NPM1* | *NRAS* | *NSD1* | *NTRK1* | *NTRK2* | *NTRK3* | *NUP93* | *PAK3* |
| *PALB2* | *PARK2* | *PAX5* | *PBRM1* | *PDCD1LG2* | *PDGFRA* | *PDGFRB* | *PDK1* | *PIK3C2B* | *PIK3CA* |
| *PIK3CB* | *PIK3CG* | *PIK3R1* | *PIK3R2* | *PLCG2* | *PMS2* | *POLD1* | *POLE* | *PPP2R1A* | *PRDM1* |
| *PREX2* | *PRKAR1A* | *PRKCI* | *PRKDC* | *PRSS8* | *PTCH1* | *PTEN* | *PTPN11* | *QKI* | *RAC1* |
| *RAD50* | *RAD51* | *RAF1* | *RANBP2* | *RARA* | *RB1* | *RBM10* | *RET* | *RICTOR* | *RNF43* |
| *ROS1* | *RPTOR* | *RUNX1* | *RUNX1T1* | *SDHA* | *SDHB* | *SDHC* | *SDHD* | *SETD2* | *SF3B1* |
| *SLIT2* | *SMAD2* | *SMAD3* | *SMAD4* | *SMARCA4* | *SMARCB1* | *SMO* | *SNCAIP* | *SOCS1* | *SOX10* |
| *SOX2* | *SOX9* | *SPEN* | *SPOP* | *SPTA1* | *SRC* | *STAG2* | *STAT3* | *STAT4* | *STK11* |
| *SUFU* | *SYK* | *TAF1* | *TBX3* | *TERC* | *TERT (promoter only)* | *TET2* | *TGFBR2* | *TNFAIP3* | *TNFRSF14* |
| *TOP1* | *TOP2A* | *TP53* | *TSC1* | *TSC2* | *TSHR* | *U2AF1* | *VEGFA* | *VHL* | *WISP3* |
| *WT1* | *XPO1* | *ZBTB2* | *ZNF217* | *ZNF703* | | | | | |

**DNA GENE LIST: FOR THE DETECTION OF SELECT REARRANGEMENTS**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *ALK* | *BCL2* | *BCR* | *BRAF* | *BRCA1* | *BRCA2* | *BRD4* | *EGFR* | *ETV1* | *ETV4* |
| *ETV5* | *ETV6* | *FGFR1* | *FGFR2* | *FGFR3* | *KIT* | *MSH2* | *MYB* | *MYC* | *NOTCH2* |
| *NTRK1* | *NTRK2* | *PDGFRA* | *RAF1* | *RARA* | *RET* | *ROS1* | *TMPRSS2* | | |

**ADDITIONAL GENOMIC SIGNATURES**

*Microsatellite status*

*Tumor Mutational Burden*

# Performance Specifications

## FOUNDATIONONE PERFORMANCE SPECIFICATIONS

| | | |
|---|---|---|
| **ACCURACY** | | |
| **Sensitivity: Base Substitutions** | At Mutant Allele Frequency ≥10% | >99.9% (CI* 99.6%-100%) |
| | At mutant Allele Frequency 5-10% | 99.3% (CI* 98.3%-99.8%) |
| **Sensitivity: Insertions/Deletions (1-40 bp)** | At Mutant Allele Frequency ≥20% | 97.9% (CI* 92.5%-99.7%) |
| | At mutant Allele Frequency 10-20% | 97.3% (CI* 90.5%-99.7%) |
| **Sensitivity: Copy Number Alterations-Amplifications** (ploidy <4, Amplification with Copy Number ≥8) | At ≥30% tumor nuclei | >99.0% (CI* 93.6%-100%) |
| | At 20% tumor nuclei | 92.6% (CI* 66.1%-99.8%) |
| **Sensitivity: Copy Number Alterations-Deletions** (ploidy <4, Homozygous Deletions) | At ≥30% tumor nuclei | 97.2% (CI* 85.5%-99.9%) |
| | At 20% tumor nuclei | 88.9% (CI* 51.8%-99.7%) |
| **Sensitivity: Rearrangements** (selected rearrangements in specimens with ≥20% tumor nuclei)** | | >90.0%[1]<br>>99.0% for ALK fusion [2] (CI* 89.1%-100%) |
| **Sensitivity: Microsatellite status** | At ≥20% tumor nuclei | 97.0% (CI* 89.6%-99.6%) |
| **Specificity: all variant types** | Positive Predictive Value (PPV) | >99.0% |
| **Specificity: Microsatellite status** | Positive Predictive Value (PPV) | >95.0% |
| **Accuracy: Tumor Mutational Burden** | At ≥20% tumor nuclei | >90.0% |
| **REPRODUCIBILITY** (average concordance between replicates) | | 96.4% inter-batch precision<br>98.9% intra-batch precision<br>95.8% microsatellite status precision<br>96.4% tumor mutational burden precision |

*95% Confidence Interval

**Performance for gene fusions within targeted introns only. Sensitivity for gene fusions occuring outside targeted introns or in highly repetitive intronic sequence contexts is reduced.

[1]Based on analysis of coverage and rearrangements structure in the COSMIC database for the solid tumor fusion genes where alteration prevalence could be stablished, complemented by detection of exemplar rearrangements in cell line tiration experiments.

[2]Based on ALK rearrangement concordance analysis vs. a standard clinical FISH assay described in: Yelensky, R. et al. Analytical validation of solid tumor fusion gene detection in a comprehensive NGS-based clinical cancer genomic test, In: Proceedings of the 105th Annual Meeting of the American Association for Cancer Research; 2014 Apr 5-9; San Diego, CA. Philadelphia (PA): AACR; 2014. Abstract nr 4699

Based on analytic validation of ROS1 gene coverage in the FoundationOne assay, the sensitivity of ROS1 rearrangement detection is estimated to be approximately 90%

Assay specifications were determined for typical median exon coverage of approximately 500X. For additional information regarding the validation FoundationOne, please refer to the article, Frampton, GM. et al. Development and validation of a clinical cancer genomic profiling test based on massively parallel DNA sequencing, Nat Biotechnol (2013 Oct. 20).

Microsatellite status, which is a measure of microsatellite instability (MSI), is determined by assessing indel characteristics at 114 homopolymer repeat loci in or near the targeted gene regions of the FoundationOne test. Microsatellite status is assayed for all FoundationOne samples and may be reported as "MSI-High", "MSI-Intermediate", "MS-Stable", or "Cannot Be Determined". Microsatellite status is reported as "Cannot Be Determined" if the sample is not of sufficient quality to be confidently determined.

Tumor Mutational Burden (TMB) is determined by measuring the number of somatic mutations occurring in sequenced genes on the FoundationOne and FoundationOne Heme tests and extrapolating to the genome as a whole. TMB is assayed for all FoundationOne and FoundationOne Heme samples and may be reported as "MSI-High", "MSI- Intermediate", "TMB-Low", or "Cannot Be Determined". TMB results, wich are rounded to the nearest integer, are determined as follows: TMB-High corresponds to greater than or equal to 20 mutations per megabase

(Muts/Mb); TMB-Intermediate corresponds to 6-19 Muts/Mb; TMB-Low corresponds to fewer than or equal to 5 Muts/Mb. Tumor Mutational Burden is reported as "Cannot Be Determined" if the sample is not of sufficient quality to confidently determine Tumor Mutational Burden

Reference Sequence Info: Sequence data is mapped to the human genome (hg19).

## Test Principle

FoundationOne® was developed and performance characteristics determined by Foundation Medicine, Inc. FoundationOne uses the T7 bait set to detect substitutions, insertion and deletion alterations (indels) and copy number alterations (CNAs) in 315 genes, and select gene rearrangements, as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB) using DNA isolated from formalin-fixed paraffin-embedded (FFPE) tumor tissue specimens.

FoundationOne has not been cleared or approved by the U.S Food and Drug Administration.
FoundationOne may be used for clinical purposes and should not be regarded as purely investigational or for research use 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 and Subclonal)

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® for identifying a copy number amplification is four (4) for ERBB2 and six (6) for all other genes. An alteration denoted as "subclonal" is one that the FoundationOne® analytical methodology has identified as being present in <10% of the assayed tumor DNA.

## Warnings and Precautions

1. Alterations reported may include somatic (not inherited) or germline (inherited) alterations; however, the test does not distinguish between germline and somatic alterations. The test does not provide information about susceptibility.
2. Biopsy may pose a risk to the patient when archival tissue is not available for use with the assay. The patient's physician should determine whether the patient is a candidate for biopsy.

## 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 judgment 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.