STUDY

Partner Name Pfizer Inc.
Partner Study ID C3441021
FMI Study ID F1S-BPA-PRO-17-625

TEST

FMI Test Order # ORD-0941933-01
Test Type FoundationOne DX1
Report Date 13 Nov 2020

PATIENT

Subject ID 12592014
Site ID 1259
Sex Male
Date of Birth 01JAN1949
Diagnosis Prostate acinar adenocarcinoma
Physician Name Not Provided

SPECIMEN

Specimen ID 6209901099
Sample Type Slide Deck
Site Prostate
Collection Date 29MAY2019
Received Date 02NOV2020
Visit Type Archival Tumor Tissue

About the Test:

FoundationOne$_{DX1}$ is a next generation sequencing assay based on the FoundationOne®CDx FDA approved platform using the DX1 bait set to detect substitutions, insertions and deletion alterations (indels) and copy number alterations (CNAs) in 324 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.

This is a QUALIFIED report. Sensitivity for the detection of alterations is reduced due to sample quality.

GENOMIC FINDINGS

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

GENE	ALTERATION
PIK3CA	E542K

GENOMIC SIGNATURES

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

Biomarker	Result
Tumor Mutational Burden	0.00 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
MSH3	A438V
MYC	E137Q
TSC1	M1067R

APPENDIX

Gene List

FoundationOne® CDx CTA is designed to include genes known to be somatically altered in human solid tumors that are validated targets for therapy, either approved or in clinical trials, and/or that are unambiguous drivers of oncogenesis based on current knowledge. The current assay interrogates 324 genes as well as introns of 36 genes involved in rearrangements. The assay will be updated periodically to reflect new knowledge about cancer biology.

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

ABL1	*ACVR1B*	*AKT1*	*AKT2*	*AKT3*	*ALK*	*ALOX12B*	*AMER1 (FAM123B)*	*APC*
AR	*ARAF*	*ARFRP1*	*ARID1A*	*ASXL1*	*ATM*	*ATR*	*ATRX*	*AURKA*
AURKB	*AXIN1*	*AXL*	*BAP1*	*BARD1*	*BCL2*	*BCL2L1*	*BCL2L2*	*BCL6*
BCOR	*BCORL1*	*BRAF*	*BRCA1*	*BRCA2*	*BRD4*	*BRIP1*	*BTG1*	*BTG2*
BTK	*C11orf30 (EMSY)*	*C17orf39 (GID4)*	*CALR*	*CARD11*	*CASP8*	*CBFB*	*CBL*	*CCND1*
CCND2	*CCND3*	*CCNE1*	*CD22*	*CD274 (PD-L1)*	*CD70*	*CD79A*	*CD79B*	*CDC73*
CDH1	*CDK12*	*CDK4*	*CDK6*	*CDK8*	*CDKN1A*	*CDKN1B*	*CDKN2A*	*CDKN2B*
CDKN2C	*CEBPA*	*CHEK1*	*CHEK2*	*CIC*	*CREBBP*	*CRKL*	*CSF1R*	*CSF3R*
CTCF	*CTNNA1*	*CTNNB1*	*CUL3*	*CUL4A*	*CXCR4*	*CYP17A1*	*DAXX*	*DDR1*
DDR2	*DIS3*	*DNMT3A*	*DOT1L*	*EED*	*EGFR*	*EP300*	*EPHA3*	*EPHB1*
EPHB4	*ERBB2*	*ERBB3*	*ERBB4*	*ERCC4*	*ERG*	*ERRFI1*	*ESR1*	*EZH2*
FAM46C	*FANCA*	*FANCC*	*FANCG*	*FANCL*	*FAS*	*FBXW7*	*FGF10*	*FGF12*
FGF14	*FGF19*	*FGF23*	*FGF3*	*FGF4*	*FGF6*	*FGFR1*	*FGFR2*	*FGFR3*
FGFR4	*FH*	*FLCN*	*FLT1*	*FLT3*	*FOXL2*	*FUBP1*	*GABRA6*	*GATA3*
GATA4	*GATA6*	*GNA11*	*GNA13*	*GNAQ*	*GNAS*	*GRM3*	*GSK3B*	*H3F3A*
HDAC1	*HGF*	*HNF1A*	*HRAS*	*HSD3B1*	*ID3*	*IDH1*	*IDH2*	*IGF1R*
IKBKE	*IKZF1*	*INPP4B*	*IRF2*	*IRF4*	*IRS2*	*JAK1*	*JAK2*	*JAK3*
JUN	*KDM5A*	*KDM5C*	*KDM6A*	*KDR*	*KEAP1*	*KEL*	*KIT*	*KLHL6*
KMT2A (MLL)	*KMT2D (MLL2)*	*KRAS*	*LTK*	*LYN*	*MAF*	*MAP2K1 (MEK1)*	*MAP2K2 (MEK2)*	*MAP2K4*
MAP3K1	*MAP3K13*	*MAPK1*	*MCL1*	*MDM2*	*MDM4*	*MED12*	*MEF2B*	*MEN1*
MERTK	*MET*	*MITF*	*MKNK1*	*MLH1*	*MPL*	*MRE11A*	*MSH2*	*MSH3*
MSH6	*MST1R*	*MTAP*	*MTOR*	*MUTYH*	*MYC*	*MYCL (MYCL1)*	*MYCN*	*MYD88*
NBN	*NF1*	*NF2*	*NFE2L2*	*NFKBIA*	*NKX2-1*	*NOTCH1*	*NOTCH2*	*NOTCH3*
NPM1	*NRAS*	*NSD3 (WHSC1L1)*	*NT5C2*	*NTRK1*	*NTRK2*	*NTRK3*	*P2RY8*	*PALB2*
PARK2	*PARP1*	*PARP2*	*PARP3*	*PAX5*	*PBRM1*	*PDCD1 (PD-1)*	*PDCD1LG2 (PD-L2)*	*PDGFRA*
PDGFRB	*PDK1*	*PIK3C2B*	*PIK3C2G*	*PIK3CA*	*PIK3CB*	*PIK3R1*	*PIM1*	*PMS2*
POLD1	*POLE*	*PPARG*	*PPP2R1A*	*PPP2R2A*	*PRDM1*	*PRKAR1A*	*PRKCI*	*PTCH1*
PTEN	*PTPN11*	*PTPRO*	*QKI*	*RAC1*	*RAD21*	*RAD51*	*RAD51B*	*RAD51C*
RAD51D	*RAD52*	*RAD54L*	*RAF1*	*RARA*	*RB1*	*RBM10*	*REL*	*RET*
RICTOR	*RNF43*	*ROS1*	*RPTOR*	*SDHA*	*SDHB*	*SDHC*	*SDHD*	*SETD2*
SF3B1	*SGK1*	*SMAD2*	*SMAD4*	*SMARCA4*	*SMARCB1*	*SMO*	*SNCAIP*	*SOCS1*
SOX2	*SOX9*	*SPEN*	*SPOP*	*SRC*	*STAG2*	*STAT3*	*STK11*	*SUFU*
SYK	*TBX3*	*TEK*	*TET2*	*TGFBR2*	*TIPARP*	*TNFAIP3*	*TNFRSF14*	*TP53*
TSC1	*TSC2*	*TYRO3*	*U2AF1*	*VEGFA*	*VHL*	*WHSC1*	*WT1*	*XPO1*
XRCC2	*ZNF217*	*ZNF703*						

DNA GENE LIST: FOR THE DETECTION OF SELECT REARRANGEMENTS

ALK	*BCL2*	*BCR*	*BRAF*	*BRCA1*	*BRCA2*	*CD74*	*EGFR*	*ETV4*
ETV5	*ETV6*	*EWSR1*	*EZR*	*FGFR1*	*FGFR2*	*FGFR3*	*KIT*	*KMT2A (MLL)*
MSH2	*MYB*	*MYC*	*NOTCH2*	*NTRK1*	*NTRK2*	*NUTM1*	*PDGFRA*	*RAF1*

RARA ***RET*** ***ROS1*** ***RSPO2*** ***SDC4*** ***SLC34A2*** ***TERC**** ***TERT***** ***TMPRSS2***

*TERC is an NCRNA

**Promoter region of TERT is interrogated

ADDITIONAL GENOMIC SIGNATURES
Loss of Heterozygosity (LOH) score
Microsatellite (MS) status
Tumor Mutational Burden (TMB)

Performance Specifications

The performance specifications of the FoundationOne® CDx CTA assay are equivalent to the FDA approved FoundationOne® CDx device. Refer to the FoundationOne CDx device for additional information.

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

Test Principle

FoundationOne® CDx CTA was developed and performance characteristics determined by Foundation Medicine, Inc. FoundationOne CDx CTA uses the DX1 bait set to detect substitutions, insertions and deletion alterations (indels) and copy number alterations (CNAs) in 324 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.

The results in this report were generated using the same reagents, equipment, procedures, final quality criteria, and variant analysis software used in the FoundationOne CDx FDA approved assay. However, a different reporting software was used to generate this report, and as a result, this assay is a laboratory developed test. It has not been cleared or approved by the U.S Food and Drug Administration. FoundationOne CDx CTA 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® CDx CTA 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 CDx CTA 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.

Limitations

1. For in vitro diagnostic use.
2. A negative result does not rule out the presence of a mutation that is below the limits of detection of the assay.
3. Samples with <30% tumor may have decreased sensitivity for the detection of CNAs including ERBB2.
4. Concordance with other validated methods for CNA (with the exception of ERBB2 amplifications and BRCA1/2 homozygous deletions) and gene rearrangement (with the exception of ALK) detection has not been demonstrated and will be provided in the post-market setting. Confirmatory testing using a clinically validated assay should be performed for all CNAs and rearrangements not associated with CDx claims noted in Table 1 of the Intended Use, but used for clinical decision making.
5. The MSI-H/MSS designation by FMI FoundationOne® CDx CTA test is based on genome wide analysis of 95 microsatellite loci and not based on the 5 or 7 MSI loci described in current clinical practice guidelines. Refer https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170019B.pdf for additional details on methodology. The threshold for MSI-H/MSS was determined by analytical concordance to comparator assays (IHC and PCR) using uterine, cecum and colorectal cancer FFPE tissue. Patients with microsatellite status of "Cannot Be Determined" should be retested with an orthogonal (alternative) method. The clinical validity of the qualitative MSI designation has not been established. For Microsatellite Instability (MSI) results, confirmatory testing using a validated orthogonal method should be considered.
6. TMB by FoundationOne CDx CTA is defined based by counting the total number of all synonymous and non-synonymous variants present at 5% allele frequency or greater (after filtering) and reported as mutations per megabase (mut/Mb) unit. TMB is a function of the characteristics of a patient's specimen and testing parameters; therefore, TMB may differ among specimens (e.g., primary vs. metastatic, tumor content) and targeted panels. The TMB calculation may differ from TMB calculations used by other assays depending on variables such as the amount of genome interrogated, percentage of tumor, assay LoD, filtering of alterations included in the score, and the read depth and other bioinformatic test specifications. Refer to the SSED for a detailed description of these variables in FMI's TMB calculation https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170019B.pdf. The clinical validity of TMB defined by this panel has not been established.
7. 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.

8. The test is intended to be performed on specific serial number-controlled instruments by Foundation Medicine, Inc.
9. Alterations in polyT homopolymer runs may not be reliably detected in BRCA1/2.
10. Certain large rearrangements in BRCA1/2 including large scale genomic deletions (affecting at least one whole exon), insertions or other deleterious genomic rearrangements including inversions or transversion events, may not be detected in an estimated 5% of ovarian cancer patients with BRCA1/2 mutations by FoundationOne CDx CTA.
11. Alterations at allele frequencies below the established limit of detection may not be detected consistently.
12. Detection of LOH has been verified only for ovarian cancer patients
13. Performance of the LOH classification has not been established for samples below 35% tumor content and with LOH scores near the cut-off of 16.
14. There may be potential interference of ethanol with LOH detection. The interfering effects of xylene, hemoglobin, and triglycerides on the LOH score have not been demonstrated.

Treatment Decisions Are 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 test, 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.