Clinical Trial Information / Patient Information

Partner Name
Partner Study ID
FMI Study ID
Site
Patient Sex Female
Patient Date of Birth

Sample Information

Accession Number
Diagnosis Lung Cancer
Received Date
Visit Type
Date Collected
Sample Type Slide Deck

For Microsatellite Instability (MSI) Results, confirmatory testing using a validated orthogonal method should be performed.

Enrollment Eligible Alterations

GENE	ALTERATION
No Eligible Variants Detected	

Electronically signed by Claire Edgerly MD. | 04 March 2020 | Foundation Medicine, Inc. |1.888.988.3639
Julia Elvin, M.D., Ph.D., Laboratory Director, CLIA: 22D2027531

Sample Preparation: 150 Second St., Cambridge, MA 02141-CLIA: 22D2027531
Sample Analysis: 150 Second St., Cambridge, MA 02141-CLIA: 22D2027531
Post-Sequencing Analysis: 150 Second St., Cambridge, MA 02141-CLIA: 22D2027531

Genomic Alterations Identified

GENE	ALTERATION
ARID1A	M1634fs*14
BRAF	BRAF-AGK fusion
CCNE1	amplification
EGFR	L858R

Variants of Unknown Significance Identified

GENE	ALTERATION
ATM	M1131I
ATRX	D980G
ATRX	L647I
BRCA2	G2901D
CALR	K368del
HSD3B1	T328S
IGF1R	E229K
INPP4B	D762V
JAK2	I899T
MLL	F2437Y
MLL	G2892A
RAC1	amplification

Advanced Genomic Analysis

Biomarker	Status/Score
TMB	8.83
MSI	MSI-Stable

FOUNDATION 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] >99.0% for ALK fusion2 (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 Mutation Burden	At ≥20% tumor nuclei	>90%
REPRODUCIBILITY (average concordance between replicates)		96.4% inter-batch precision 98.9% intra-batch precision 95.8% microsatellite status precision 96.4% tumor mutation burden precision
Loss of heterozygosity: Performance of LOH in this assay has been shown to be equivalent to performance of FoundationFocus BRCA LOH. Performance details can be found at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P160018S001. Samples with <35% tumor may have decreased sensitivity for LOH score determination.		

* 95% Confidence Interval

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

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

Assay specifications were determined for typical median exon coverage of approximately 500X. For additional information regarding the validation of 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 (a measure of microsatellite instability, or "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. MSI-High results are reported in all tumor types. In select tumor types, other Microsatellite status results may be reported (MS-Stable, MSI-Ambiguous, MSI-Unknown) when relevant. Microsatellite status result may be reported as "Unknown" if the sample is not of sufficient quality to confidently determine Microsatellite status.

Tumor Mutation 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. TMB-High results are reported in all tumor types. In select tumor types, other TMB results may be reported (TMB-Intermediate, TMB-Low, TMB-Unknown) when relevant. TMB results 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 less than or equal to 5 Muts/Mb. Tumor Mutation Burden may be reported as "Unknown" if the sample is not of sufficient quality to confidently determine Tumor Mutation Burden.

[II]Reduced Sensitivity: Although we can definitively confirm the presence of the genomic alterations detailed in this report, the data obtained may have been insufficient for comprehensive detection of genomic alterations. Reduced sensitivity may be due to poor sample quality or, in rare cases, to patient transplant history. Any Tumor Mutation Burden (TMB) value (Muts/Mb) shown on a report with reduced sensitivity reflects an estimate of the lowest possible TMB.

Gene List

Genes Assayed in DX1:

ABL1	ACVR1B	AKT1	AKT2	AKT3
ALK	ALOX12B	APC	AR	ARAF
ARFRP1	ARID1A	ASXL1	ATM	ATR
ATRX	AURKA	AURKB	AXIN1	AXL
BAP1	BARD1	BCL2	BCL2L1	BCL2L2
BCL6	BCOR	BCORL1	BCR	BRAF
BRCA1	BRCA2	BRD4	BRIP1	BTG1
BTG2	BTK	C17orf39	CALR	CARD11
CASP8	CBFB	CBL	CCND1	CCND2
CCND3	CCNE1	CD22	CD274	CD70
CD74	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	EMSY	EP300	EPHA3
EPHB1	EPHB4	ERBB2	ERBB3	ERBB4
ERCC4	ERG	ERRFI1	ESR1	ETV4
ETV5	ETV6	EWSR1	EZH2	EZR
FAM123B	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	KRAS
LTK	LYN	MAF	MAP2K1	MAP2K2
MAP2K4	MAP3K1	MAP3K13	MAPK1	MCL1
MDM2	MDM4	MED12	MEF2B	MEN1
MERTK	MET	MITF	MKNK1	MLH1
MLL	MLL2	MPL	MRE11A	MSH2
MSH3	MSH6	MST1R	MTAP	MTOR
MUTYH	MYB	MYC	MYCL1	MYCN
MYD88	NBN	NF1	NF2	NFE2L2
NFKBIA	NKX2-1	NOTCH1	NOTCH2	NOTCH3
NPM1	NRAS	NT5C2	NTRK1	NTRK2
NTRK3	NUTM1	P2RY8	PALB2	PARK2
PARP1	PARP2	PARP3	PAX5	PBRM1
PDCD1	PDCD1LG2	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	RSPO2	SDC4
SDHA	SDHB	SDHC	SDHD	SETD2
SF3B1	SGK1	SLC34A2	SMAD2	SMAD4
SMARCA4	SMARCB1	SMO	SNCAIP	SOCS1
SOX2	SOX9	SPEN	SPOP	SRC
STAG2	STAT3	STK11	SUFU	SYK
TBX3	TEK	TERC	TERT	TET2
TGFBR2	TIPARP	TMPRSS2	TNFAIP3	TNFRSF14
TP53	TSC1	TSC2	TYRO3	U2AF1
VEGFA	VHL	WHSC1	WHSC1L1	WT1
XPO1	XRCC2	ZNF217	ZNF703	

Genes Assayed in the Foundation Medicine Assay

The current Foundation Medicine assay is designed to include all 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 assay will be updated periodically to reflect new knowledge about cancer biology.