Admera Health, LLC
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PATIENT INFORMATION		SAMPLE INFORMATION		REFERING PHYSICIAN	COPY TO (if different from ordering)
Name:	Someone	Date Collected:	11/10/2018	Name:	Name:
DOB:		Date Received:	11/11/2018	Institution:	Institution:
Age:	51	Date of Report:	11/18/2018	Address:	Address:
Sex:	Male	lab ID:	N-000682		
Address:	South Plainfield, NJ, 07080	Testing Method:	NGS	Contact:	Contact:

Tumor Profile for Someone

ICD-10: C34.90: Non-Small Cell Lung Cancer (NSCLC)

OncoGxOne™

Result: POSITIVE

Mutations Detected: EGFR-G719A, KRAS-G12D, MET-Amplification
MSI: MSI-UNSTABLE
TMB: TMB-HIGH
Clinical Trials Available: Yes

Medically Actionable Alterations

THERAPIES LINKED TO VARIANTS OF KNOWN CLINICAL SIGNIFICANCE

Gene	Molecular Abnormality	Therapies	Approved For	Allele Freq	LOE
EGFR	G719A	Erlotinib, Gefitinib	NSCLC	23.50%	A
KRAS	G12D	Trametinib	NSCLC	20.50%	B
MET	Amplification	Crizotinib	NSCLC	NA	A

THERAPIES LINKED TO RESISTANCE VARIANTS OF KNOWN CLINICAL SIGNIFICANCE

Gene	Molecular Abnormality	Therapies	Approved For	Allele Freq	LOE
KRAS	G12D	Erlotinib, Gefitinib	NSCLC	20.50%	A
MET	Amplification	Erlotinib, Gefitinib	NSCLC	NA	A

LOE: Therapeutic-level-of-evidence, definition of LOE shown in Table 1.

THERAPIES LINKED TO VARIANTS OF POTENTIAL CLINICAL SIGNIFICANCE

Gene	Molecular Abnormality	Therapies	Approved For	Allele Freq	LOE
KRAS	G12D	Selumetinib	Thyroid Cancer	20.50%	C
KRAS	G12D	MK-2206	Pancreatic Carcinoma	20.50%	C
KRAS	G12D	Selumetinib+BEZ235	Colorectal Cancer	20.50%	D
MET	Amplification	Cabozantinib	Thyroid Cancer	NA	C
MET	Amplification	Vemurafenib+Crizotinib	Colorectal Cancer	NA	C
MET	Amplification	Onartuzumab	Gastric Adenocarcinoma	NA	C
MET	Amplification	Crizotinib	Glioblastoma Multiforme	NA	C
MET	Amplification	Cetuximab+Crizotinib	Colorectal Cancer	NA	C

Table 1: Definitions of Levels of Evidence

Known Clinical Significance	**Level A**	Therapy is FDA-approved or recommended in professional guidelines.
	Level B	Therapy is supported by well-powered studies with consensus from experts in the field.
Potential Clinical Significance	**Level C**	Therapy is FDA-approved for different tumor types (off-label use) or supported by multiple small published studies or case studies.
	Level D	Therapy is supported by preclinical study or studies.

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MICROSATELLITE INSTABILITY (MSI)

MSI Result: MSI-UNSTABLE

MICROSATELLIIT INSTABILITY (MSI)						
BAT-25	BAT-26	NR-21	NR-24	NR-27	Therapies	Tumor Type
Positive	Positive	Positive	Negative	Negative	Pembrolizumab	NSCLC

TUMOR MUTATION BURDEN (TMB) PREDICTION

TMB Result: TMB-HIGH

TUMOR MUTATION BURDEN (TMB)			
Mutations / Mega base	Results	Therapies	Tumor Type
15	High	Nivolumab + Ipilimumab or Nivolumab	NSCLC

INFORMATION OF HLA GENOTYPING DETECTED

The human leukocyte antigen (HLA) system is a gene complex encoding the major histocompatibility complex (MHC) proteins in humans. It is responsible for the regulation of the immune system in humans. Patients' HLA genotypes may influence how well they respond to immunotherapy.

HLA GENOTYPING							
Gene	Allele 2	Allele 2	Genotype	Gene	Allele 2	Allele 2	Genotype
HLA-A	2402	2402	**Homozygous**	***HLA-DPA1***	0104	0104	**Homozygous**
HLA-B	5201	5201	**Homozygous**	***HLA-DPB1***	0401	0401	**Homozygous**
HLA-C	2402	1202	**Heterozygous**	***HLA-DQA1***	0501	0501	**Heterozygous**
HLA- DMA	0101	0101	**Homozygous**	***HLA-DQB1***	0201	0301	**Heterozygous**
HLA- DMB	0101	0101	**Homozygous**	***HLA-DRA***	0101	0102	**Heterozygous**
HLA- DOA	0101	0102	**Heterozygous**	***HLA-DRB1***	0301	0408	**Heterozygous**
HLA- DOB	0101	0104	**Heterozygous**	***HLA-DRB5***	0104	0104	**Homozygous**

CLINICAL TRIALS TO CONSIDER

1. EGFR G719A Associated Clinical Trials

Therapies	NCT ID	Title	Phase	Locations#
Osimertinib	NCT03434418	A Study Osimertinib in Patients With Stage 4 Non-small Cell Lung Cancer With Uncommon EGFR Mutations	2	North Carolina
Osimertinib Sapanisertib	NCT02503722	A Study Osimertinib in Patients With Stage 4 Non-small Cell Lung Cancer With Uncommon EGFR MutationsSapanisertib and Osimertinib in Treating Patients With Stage IV EGFR Mutation Positive Non-small Cell Lung Cancer After Progression on a Previous EGFR Tyrosine Kinase Inhibitor	1	Connecticut
Osimertinib Navitoclax	NCT02520778	Osimertinib and Navitoclax in Treating Patients With EGFR-Positive Previously Treated Advanced or Metastatic Non-small Cell Lung Cancer	1	California
Osimertinib Necitumumab	NCT02496663	Osimertinib and Necitumumab in Treating Patients With EGFR-Mutant Stage IV or Recurrent Non-small Cell Lung Cancer Who Have Progressed on a Previous EGFR Tyrosine Kinase Inhibitor	1	California

2. KRAS G12D Associated Clinical Trials

Therapies	NCT ID	Title	Phase	Locations#
Bortezomib Acyclovir	NCT01833143	Bortezomib in KRAS-Mutant Non-Small Cell Lung Cancer in Never Smokers or Those With KRAS G12D	2	New Jersey New York
Docetaxel Trametinib	NCT02642042	Trametinib and Docetaxel in Treating Patients With Recurrent or Stage IV KRAS Mutation Positive Non-small Cell Lung Cancer	2	Alaska Arkansas
Carboplatin Paclitaxel Trametinib	NCT01912625	Trametinib, Combination Chemotherapy, and Radiation Therapy in Treating Patients With Stage III Non-small Cell Lung Cancer That Cannot Be Removed by Surgery	1	Minnesota Ohio
ARQ 197 plus erlotinib Pemetrexed, docetaxel or gemcitabine	NCT01395758	rlotinib Plus Tivantinib (ARQ 197) Versus Single Agent Chemotherapy in Locally Advanced or Metastatic Non-Small Cell Lung Cancer	2	California Florida
Trametinib Ponatinib	NCT03704688	Trial of Trametinib and Ponatinib in Patients With KRAS Mutant Advanced Non-Small Cell Lung Cancer	1/2	New York

3. MET Amplification Associated Clinical Trials				
Therapies	**NCT ID**	**Title**	**Phase**	**Locations#**
Sym015	NCT02648724	Sym015 (Anti-MET) in Patients With Advanced Solid Tumor Malignancies	1/2	Colorado
INC280 INC280 + Erlotinib Platinum/pemetrexed	NCT02468661	A Safety and Efficacy Study of INC280 Alone, and in Combination With Erlotinib, Compared to Chemotherapy, in Advanced/Metastatic Non-small Cell Lung Cancer Patients With EGFR Mutation and cMET Amplification	1	Connecticut
Tepotinib	NCT02864992	Tepotinib Phase II in Non-small Cell Lung Cancer (NSCLC) Harboring MET Alterations (VISION)	2	California, Colorado
JNJ-61186372	NCT02609776	Study of JNJ-61186372, a Human Bispecific EGFR and cMet Antibody, in Participants With Advanced Non-Small Cell Lung Cancer	1	California Florida
Osimertinib Savolitinib	NCT03778229	Osimertinib Plus Savolitinib in EGFRm+/MET+ NSCLC Following Prior Osimertinib (SAVANNAH)	2	California Massachusetts

 # The two locations closest to the patient's address based on zip code are shown (for US locations, otherwise show all locations).
Note: Select clinical trials are shown. For a full list of clinical trials, please search the ClinicalTrials.gov website.

ABOUT GENES, MSI, and TMB

EGFR

The protein encoded by this gene is a transmembrane glycoprotein that is a member of the protein kinase superfamily. This protein is a receptor for members of the epidermal growth factor family. EGFR is a cell surface protein that binds to epidermal growth factor. Binding of the protein to a ligand induces receptor dimerization and tyrosine autophosphorylation and leads to cell proliferation. Mutations in this gene are associated with lung cancer.

Mutation prevalence

EGFR mutations have been reported in 27% (25179/93101) of Non-small cell lung carcinoma (NSCLC) samples analyzed in COSMIC (Jan 2019).

Effect of mutation

EGFR-G719A is an activating mutation. EGFR activating mutations or amplification may predict sensitivity to Egfr targeted therapies, including inhibitors of multiple ErbB family members, and several have received FDA approva in some tumor types (Mok et al., 2009; 19692680, Rosell et al., 2009; 19692684, Tsao et al., 2005; 16014883). Many of the less commonly observed alterations in EGFR, which cumulatively account for ~10% of EGFR-mutated NSCLC (ie, exon 19 insertions, p.L861Q, p.G719X, p.S768I) are also associated with responsiveness to EGFR TKI therapy, although the number of studied patients is lower than the most commonly described mutations in EGFR (exon 19 deletions, p.L858R point mutation in exon 21)(NCCN v.3.2019).The NCCN Panel recommends erlotinib and gefitinib (category 1) as first-line therapy in patients with advanced, recurrent, or metastatic nonsquamous NSCLC who have known active sensitizing EGFR mutations based on these trials and FDA approvals(Eberhard et al., 2005; 16043828, Mok et al., 2009; 19692680, Sequist et al., 2007; 17285735, Inoue et al., 2009; 19224850).

KRAS

This gene, a Kirsten ras oncogene homolog from the mammalian ras gene family, encodes a protein that is a member of the small GTPase superfamily. A single amino acid substitution is responsible for an activating mutation. The transforming protein that results is implicated in various malignancies, including lung adenocarcinoma, mucinous adenoma, ductal carcinoma of the pancreas and colorectal carcinoma. Alternative splicing leads to variants encoding two isoforms that differ in the C-terminal region.

Mutation prevalence

KRAS mutations have been reported in 6.82%(306/4488) of Non-small cell lung carcinoma (NSCLC) samples analyzed in COSMIC (Jan 2019).

Effect of mutation

KRAS encodes the signaling protein K-Ras,a member of the Ras family; activating KRAS alterations may result in activation of downstream signaling pathways,including the Raf/MEK/ERK pathway (Pylayeva-Gupta et al., 2011; 21993244, Nakano et al., 1984; 6320174). Point mutations in KRAS most commonly occur at codon 12. KRAS-G12D is an activating mutation. KRAS mutational status is predictive of lack of therapeutic efficacy with EGFR TKIs; it does not appear to affect chemotherapeutic efficacy (Eberhard et al., 2005; 16043828, Miller et al., 2008; 18349398, Roberts et al., 2013; 23401440). Several MEK inhibitors are under clinical investigation, including the FDA-approved therapies trametinib and cobimetinib,and may be relevant for tumors harboring K-Ras activation (Flaherty et al., 2012; 22663011, Larkin et al.,2014; 25265494, Britten et al.,2013; 23443307,Jänne et al.,2013; 23200175). The use of NVP-BEZ235 in conjunction with ARRY-142886, but not as monotherapy, in a lung cancer model with KRAS G12D mutation led to marked tumor regression(Engelman et al., 2008; 19029981).

MET

This gene encodes a member of the receptor tyrosine kinase family of proteins and the product of the proto-oncogene MET. The encoded preproprotein is proteolytically processed to generate alpha and beta subunits that are linked via disulfide bonds to form the mature receptor. Further processing of the beta subunit results in the formation of the M10 peptide, which has been shown to reduce lung fibrosis. Binding of its ligand, hepatocyte growth factor, induces dimerization and activation of the receptor, which plays a role in cellular survival,

embryogenesis, and cellular migration and invasion. Mutations in this gene are associated with papillary renal cell carcinoma, hepatocellular carcinoma, and various head and neck cancers. Amplification and overexpression of this gene are also associated with multiple human cancers.

Mutation prevalence
MET Amplification has been reported in ~5-20% of patients with EGFR mutant tumors and acquired resistance to EGFR TKIs (Arcila et al., 2011; 21248300, Sequis et al., 2011; 21430269).

Effect of mutation
MET Amplification can lead to overexpression of the MET protein,this can further lead to cell growth,the development of new blood vessels,which are inegral to cancer development. Overexpression of MET also plays an important role in acquired resistance to EGFR inhibitors of patients with EGFR-mutated tumors (Bean et al.,2007; 18093943, Turke et al.,2010; 20129249, Engelman et al.,2007; 17463250). High-level MET amplifications or MET exon 14 skipping mutations are emerging predictive biomarkers for patients with metastatic NSCLC in the NCCN Guidelines for NSCLC (NCCN, v.3.2019). Crizotinib inhibits ALK rearrangements, ROS1 rearrangements, and some MET tyrosine kinases (high-level MET amplification or METex14 mutation); it is approved by the FDA for patients with metastatic NSCLC who have ALK gene rearrangements (ie, ALK-positive disease) or ROS1 rearrangements (Kazandjian et al., 2014; 25170012, Awad et al., 2016; 26729443, Solomon et al., 2014; 25470694, FDA, 2019). Accumulating data suggest how cancers become resistant to EGFR inhibitors (Ou et al., 2012; 22257651). Apart from EGFR T790M, which renders the kinase resistant to erlotinib, gefitinib, dacomitinib, or afatinib, amplification of the MET oncogene is another validated resistance mechanism. To overcome resistance, EGFR must still be inhibited. In the case of MET amplification, new inhibitors must be added to the EGFR inhibitor; EGFR inhibition is still required to induce remission (NCCN, v.3.2019).

MSI

Microsatellite instability (MSI) is a pattern of hypermutation that occurs at genomic microsatellites and is caused by defects in the mismatch repair system. Mismatch repair deficiency that leads to MSI has been well described in several types of human cancer, most frequently in colorectal, endometrial, and gastric adenocarcinomas. MSI is known to be both predictive and prognostic (Bonneville et al., 2017; 29850653). Pembrolizumab is a programmed death receptor-1 (PD-1)-blocking antibody indicated in combination with pemetrexed and platinum chemotherapy, as first-line treatment of patients with metastatic nonsquamous NSCLC, with no EGFR or ALK genomic tumor aberrations; in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, as first-line treatment of patients with metastatic squamous NSCLC; as a single agent for the first-line treatment of patients with stage III NSCLC, who are not candidates for surgical resection or definitive chemoradiation, or metastatic NSCLC, and whose tumors express PD-L1 [Tumor Proportion Score (TPS) ≥1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations; as a single agent for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Pembrolizumab . The U.S. Food and Drug Administration granted accelerated approval to pembrolizumab (KEYTRUDA, Merck & Co.) for adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors that have progressed following prior treatment(FDA, 2017).

TMB

Tumor mutational burden (TMB) is an evolving biomarker that may be helpful in selecting patients for immunotherapy. For the 2019 update (Version 1), the NCCN Panel recommends (category 2A) nivolumab with or without ipilimumab for patients with high TMB levels (NCCN). Nivolumab (OPDIVO) is a programmed death receptor-1 (PD-1) blocking antibody indicated for the treatment of patients with metastatic non-small cell lung cancer and progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving OPDIVO (FDA, 2019). CTLA-4 is a negative regulator of T-cell activity. Ipilimumab is a monoclonal antibody that binds to CTLA-4 and blocks the interaction of CTLA-4 with its ligands, CD80/CD86. Blockade of CTLA-4 has been shown to augment T-cell activation and proliferation, including the activation and proliferation of tumor infiltrating T-effector cells. Inhibition of CTLA-4 signaling can also reduce T-regulatory cell function, which may contribute to a general increase in T cell responsiveness, including the anti-tumor immune response (FDA, 2019).

CANCER DRUG INFORMATION

COMETRIQ® (Cabozantinib)
http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/203756lbl.pdf

XALKORI® (Crizotinib)
http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/202570s013lbl.pdf

TARCEVA® (Erlotinib)
http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/021743s018lbl.pdf

IRESSA® (Gefitinib)
http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/206995s000lbl.pdf

YERVOY® (Ipilimumab)
https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/125377s073lbl.pdf

OPDIVO® (Nivolumab)
https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/125527s000lbl.pdf

KEYTRUDA® (Pembrolizumab)
https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/125514s014lbl.pdf

MEKINIST® (Trametinib)
http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/204114s001lbl.pdf

ZELBORAF® (Vemurafenib)
http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/202429s006lbl.pdf

Table 2: OncoGxOne™ Panel Genes

OncoGxOne™ is a single-panel cancer test panel designed to provide comprehensive genomic analysis for cancer therapy. This test detects all types of genetic alterations (point mutations, small insertions/deletions, gene fusions, copy number variations) in the 364 genes listed in the table below. Gene coverage includes all coding exons and untranslated regions (UTRs), as well as select mRNA junctions known to be involved in gene fusion events.

List of OncoGxOne Panel gene names (364 genes in total, 38 sequenced from DNA and RNA in gray box)												
ABL1	BCL6	BTK	PDCD1LG2	CTNNB1	RAC1	FANCC	FGF23	SDHC	HLA-DPA1	TERT	MAP2K1	MEF2B
ACVR1B	BCOR	C11orf30	PDGFRA	CUL3	DOT1L	FANCD2	FGF3	SDHD	HLA-DPB1	TET2	MAP2K2	MEN1
AKT1	NF2	CALR	PDGFRB	CUL4A	EED	FANCF	FGF4	SETD2	HLA-DQA1	IFG1	MAP2K4	MERTK
AKT2	NFE2L2	CARD11	PDK1	CXCR4	EGFR	RAD21	FGF6	SF3B1	HLA-DQB1	IGF1R	MAP3K1	MET
AKT3	NFKBIA	CASP8	PIK3C2B	CYP17A1	EP300	RAD50	FGFR1	SGK1	HLA-DRA	IKBKE	TGFBR1	MITF
ALK	NKX2-1	CBFB	PIK3C2G	D17S250	EPHA3	RAD51	FGFR2	SLC34A2	HLA-DRB1	IKZF1	TGFBR2	MKNK1
ALOX12B	NOTCH1	CBL	PIK3CA	DAXX	EPHA5	RAD51B	FGFR3	SMAD2	HLA-DRB5	INPP4B	TIPARP	MLH1
AMER1	NOTCH2	CCND1	PIK3CB	DDR1	EPHB1	RAD51C	FGFR4	SMAD4	HNF1A	IRF2	TMPRSS2	MPL
APC	NOTCH3	CCND2	PIK3CD	DDR2	EPHB4	RAD51D	FH	SMARCA4	HRAS	IRF4	TNFAIP3	MRE11A
AR	NPM1	CCND3	PIK3R1	DIS3	ERBB2	RAD52	FLCN	SMARCB1	HSD3B1	IRS2	TNFRSF14	MSH2
ARAF	NRAS	CCNE1	CDK6	DNMT1	ERBB3	RAD54L	FLT1	SMO	ID3	JAK1	TOP1	MSH3
ARFRP1	NRG1	CD22	CDK8	DNMT3A	ERBB4	RAF1	FLT3	GID4	IDH1	JAK2	TP53	MSH6
ARID1A	NT5C2	CD274	CDKN1A	PIM1	ERCC2	RARA	FLT4	GNA11	IDH2	JAK3	TSC1	MST1R
ASXL1	NTRK1	CD70	CDKN1B	PMS1	ERCC3	RB1	FOXL2	GNA13	SNCAIP	JUN	TSC2	MTAP
ATM	NTRK2	CD74	CDKN2A	PMS2	ERCC4	RBM10	FOXO1	GNAQ	SOCS1	KDM5A	TYRO3	MTOR
ATR	NTRK3	CD79A	CDKN2B	POLD1	ERG	REL	FUBP1	GNAS	SOX2	KDM5C	U2AF1	MUTYH
ATRX	NUTM1	CD79B	CDKN2C	POLE	ERRFI1	RET	FYN	GRM3	SOX9	KDM6A	VEGFA	MYB
AURKA	P2RY8	CDC73	CEPBA	PPARG	ESR1	RICTOR	GABRA6	GSK3B	SPEN	KDR	VHL	MYC
AURKB	PALB2	CDH1	CHEK1	PPP2R1A	ETV1	RNF43	GATA3	H3F3A	SPOP	KEAP1	WHSC1	MYCL
AXIN1	BCORL1	CDK12	CHEK2	PPP2R2A	ETV4	ROS1	GATA4	HDAC1	SRC	KEL	WHSC1L1	MYCN
AXL	BCR	CDK4	CIC	PRDM1	ETV5	FANCG	GATA6	HGF	STAG2	KIT	WT1	MYD88
B2M	BRAF	PARK2	CREBBP	PRKAR1A	ETV6	FANCL	GEN1	HLA-A	STAT3	KLHL6	MAP3K13	NBN
BACH1	BRCA1	PARP1	CRKL	PRKCI	EWSR1	FAS	RPA1	HLA-B	STK11	KMT2A	MAPK1	NF1
BAP1	BRCA2	PARP2	CRLF2	PTCH1	EZH2	FBXW7	RPTOR	HLA-C	SUFU	KMT2D	MAPK3	XPO1
BARD1	BRD4	PARP3	CSF1R	PTEN	EZR	FGF10	RSPO2	HLA-DMA	SYK	KRAS	MCL1	XRCC2
BCL2	BRIP1	PAX5	CSF3R	PTPN11	FAM46C	FGF12	SDC4	HLA-DMB	TBX3	LTK	MDM2	YES1
BCL2L1	BTG1	PBRM1	CTCF	PTPRO	FAM175A	FGF14	SDHA	HLA-DOA	TEK	LYN	MDM4	ZNF217
BCL2L2	BTG2	PDCD1	CTNNA1	QKI	FANCA	FGF19	SDHB	HLA-DOB	TERC	MAF	MED12	ZNF703

References:

- NCCN Biomarkers Compendium at: http://www.nccn.org/professionals/biomarkers/content/
- U.S. Food and Drug Administration, Table of Pharmacogenomic Biomarkers in Drug Labeling. Available online at: http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm083378.htm
- My Cancer Genome at: http://www.mycancergenome.org/
- PharmGKB: The Pharmacogenomics Knowledgebase. Available online at: http://www.pharmgkb.org/index.jsp
- The Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline. Available online at: https://www.pharmgkb.org/page/cpic
- European Medicines Agency, Multidisciplinary: Pharmacogenomics. Available online at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000411.jsp∣=WC0b01ac058002958e
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Test Methodology and Limitations for OncoGxOne™:

Target regions of interest were captured using a custom probe library and sequenced by massive parallel sequencing method (Illumina platform). The detected mutations are annotated based on hg19 reference genome assembly. The OncoGxOne™ test was developed by Admera Health, including determination and validation of performance characteristics. The sensitivity and specificity of this test is greater than 98% and 97%, respectively, when a minimum of 10% tumor tissue is present in the sample. This test has not been approved by the U.S. Food and Drug Administration (FDA) and is for research purposes only. The Admera Health clinical laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), accredited by the College of American Pathologists, and is qualified to perform high complexity clinical laboratory testing.

Anti-PD-1 therapy has been FDA approved for patients classified as microsatellite instability unstable (MSI-UNSTABLE) and tumor mutation burden high (TMB-HIGH). The OncoGxOne™ test determines the status of microsatellite instability (MSI) by detecting the length of mononucleotide repeats at five genomic sites (BAT-25, BAT-26, NR-21, NR-24, and NR-27). A positive call at >= 2 sites is required for a patient to be classified as MSI-UNSTABLE. Tumor mutation burden (TMB) is a quantitative and genomic-based biomarker for cancer immunotherapy. TMB is measured by the number of somatic mutations per mega base (MB) in coding regions of tumor cells within OncoGxOne™ panel. OncoGxOne™ classifies TMB into two different categories: TMB-HIGH with mutations > 10 per MB, and TMB-LOW with mutations <= 10 per MB.

Disclaimer of Liability:

The information contained in this report is provided as a service and does not constitute medical advice. At the time of report generation this information is believed to be current and is based upon published research; however, research data evolves and amendments to the prescribing information of the drugs listed will change over time. While this report is believed to be accurate and complete as of the date issued, THE DATA IS PROVIDED "AS IS", WITHOUT WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION, THE IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE. As medical advice must be tailored to the specific circumstances of each case, the treating health care professional has ultimate responsibility for all treatment decisions made with regard to a patient including any made on the basis of a patient's genotype.

I certify that these lab results are accurate.

Signatures:

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James Dermody
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