GCG-Oncomine Comprehensive Assay Plus (TMB/MSI, incl. RNA)

Personal Information	Specimen Information	Test Information
Name: Jason Doe	Sample ID: 20221031-971-0000	Test reported: 2022-11-11
Relation: -	Medical record No: -	Ordering physician: Dr. Smith
Sex/Birth: M / 1934-12-01	Date received: 2022-10-31	Institution: Hospital A

INDICATION	Head and Neck Cancer

SUMMARY

	Tier 1	Tier 2	TMB Score	MSI Status
Variant	0	5	5.68 Mutations/Mb	MSS
Gene	-	PIK3CA, RASA1, AKT1, TP53		

QC RESULT

DNA (SNV)	DNA (CNV)	RNA	TMB	MSI
Pass	Pass	Pass	Pass	Pass

TEST

Tier 1 : Variants of Strong Clinical Significance 0

No	Gene	DNA	Protein	VAF(%)	Depth(X)	COSMIC ID
No variant						

INTERPRETATION

No Tier 1 Variant

Tier 2 : Variants of Potential Clinical Significance 5

No	Gene	DNA	Protein	VAF(%)	Depth(X)	COSMIC ID
1	PIK3CA	Amplification	5.7 copy number gain*	.	-	-
2	RASA1	c.809_815del	p.Tyr270LeufsTer7	39.5	1,954	-
3	RASA1	c.818_827del	p.Ala273GlyfsTer3	51.1	1,719	-
4	AKT1	Amplification	6.3 copy number gain*	.	-	-
5	TP53	c.742C>T	p.Arg248Trp	56.2	1,736	COSM10656

INTERPRETATION

* This copy number is calculated by assuming the tumor burden as 100%. The actual tumor copy number may be higher depending on the tumor burden.

PIK3CA gene amplification is detected. This is a likely oncogenic variant with a gain-of-function mechanism. There is no approved target therapy for this kind of tumor.

Tested by: M-K Lee M.T(20058) MKlee Confirmed by: Jong-Mun Choi M.D(924) CJM

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INTERPRETATION

A frameshift variant c.809_815del (p.Tyr270LeufsTer7, Y270Lfs*7) is detected in the RASA1 gene. Truncation variants in the RASA1 gene could be classified as a Likely Oncogenic variant with a Likely Loss-of-function mechanism. There is no approved therapy for this kind of tumor.

A frameshift variant c.818_827del (p.Ala273GlyfsTer3, A273Gfs*3) is detected in the RASA1 gene. Truncation variants in the RASA1 gene could be classified as a Likely Oncogenic variant with a Likely Loss-of-function mechanism. There is no approved therapy for this kind of tumor.

AKT1 gene amplification is detected. This is a likely oncogenic variant with a gain-of-function mechanism. There is no approved target therapy for this kind of tumor.

A missense variant c.742C>T (p.Arg248Trp, R248W) is detected in the TP53 gene. The variants is classified as a Likely Oncogenic variant with a Likely Loss-of-function mechanism. There is no approved therapy for this kind of tumor.

Tier 3 : Variants of Unknown Clinical Significance	1

No	Gene	DNA	Protein	VAF(%)	Depth(X)	COSMIC ID
1	MECOM	Amplification	7.1 copy number gain*	.	-	-

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TEST INFORMATION

1. TEST METHOD

Target Region	427 genes
Tested Panel	Solid Tumor Panel II(TMB/MSI)(RNA included)
Target Enrichment Method	Amplicon-based assay(Oncomine Comprehensive Plus)
Massively Parallel Sequencing	Ion S5
Bioinformatic Pipeline	Oncomine Comprehensive Plus - w.2.3 - DNA and Fusions - Single Sample
Reference Genome	GRCh37/hg19

2. QC DATA

DNA(SNV)			RNA(Fusion)		
Mean Target Depth(X)	2,531		Total Mapped Fusion Reads	2,187,767	>500,000
% of Target Bases ≥ 250X	97.98	>90%	Pool 1 Mapped Fusion Reads	1,070,249	>100,000
Uniformity(%)	95.23	>80%	Pool 2 Mapped Fusion Reads	1,117,518	>100,000
			cDNA qPCR ct	20.33	
DNA(CNV)			**TMB**		
MAPD	0.38	<0.5	Deamination Value	0	<60
MSI			Average Coverage	2358	>150
MSI Coverage	114,088	>50			

3. LIMITATIONS

- This test was performed using sequencing analysis, and can detect SNP and small-indel variants within the analyzed region. The test cannot detect any variants in the region not covered by the test.
- The limit of detection for SNV and small-indel variants is approximately 5%.
- The detection rate of certain regions such as homopolymer and repeat regions may be lower due to limitation of DNA sequencing method,and certain target region may have lower coverage.
- The detected variants in this test are not confirmed by Sanger sequencing, ddPCR or other confirmation methods.
- This test does not distinguish between germline and somatic variants. If the variant allele frequency of the mutation is close to 50% or 100%, the possibility of germline variant cannot be excluded.
- The variants detected in this test are classified into four stages (tier 1~4) according to the 2017 JMD guideline, and tier 4 variants are not reported.
- If the MAPD (Median of the Absolute values of all Pairwise Differences) score, a QC index for CNV calling, exceed 0.5, CNV analysis will not be performed. If the MAPD score exceed 0.3, the reliability is considered low.
- For CNV analysis, only copy number gain is reported. The detection limit of copy number gain is about 4 copy gain.
- MSI status is reported as MSI-High or MSS. If the 76 MSI biomarkers are not covered enough, MSI status may be reported as no call or QC fail. Validation of MSI status from the manufacturer,using 192 samples, showed sensitivity of 96% and specificity of 99%.
- TMB score is the number of mutations detected per 106 base pair. The classification for TMB-low and TMB-high is not yet defined.

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4. CLASSIFICATIONS

Somatic Variants are classified into four stages according to the evidence level and clinical significance of the mutation. Tier 4 is not reported.

Tier 1	Strong clinical significance	Level A and Level B evidence
Tier 2	Potential clinical significance	Level C and Level D evidence
Tier 3	Unknown clinical significance	Not observed at a significant allele frequency in the general or specific subpopulation databases, or pan-cancer or tumor-specific variant databases. No convincing published evidence of cancer association.
Tier 4	Benign or likely benign	Observed at significant allele frequency in the general or specific subpopulation databases. No existing published evidence of cancer association.

EVIDENCE LEVEL

Level A	FDA-approved therapy Included in professional guidelines.
Level B	Well-powered studies with consensus from experts in the field.
Level C	FDA-approved therapies for different tumor types or investigational therapies. Multiple small published studies with some consensus.
Level D	Preclinical trials or a few case reports without consensus.

REFERENCES

- COSMIC(http://cancer.sanger.ac.uk)
- c-bioportal(http://www.cbioportal.org)
- Cancer Hotspots(http://cancerhotspots.org)
- My Cancer Genome(https://www.mycancergenome.org/)
- The Clinical Knowledgebase(https://ckb.jax.org/)
- WHO classification of tumours of haematopoietic and lymphoid tissues(revised 4th edition)
- NCCN guidelines®

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5. GENE LIST

CDS (n=227)

ABRAXAS1	ACVR1B	ACVR2A	ADAMTS12	ADAMTS2	AMER1	APC	ARHGAP35	ARID1A	ARID1B
ARID2	ARID5B	ASXL1	ASXL2	ATM	ATR	ATRX	AXIN1	AXIN2	B2M
BAP1	BARD1	BCOR	BLM	BMPR2	BRCA1	BRCA2	BRIP1	CALR	CASP8
CBFB	CD274	CD276	CDC73	CDH1	CDH10	CDK12	CDKN1A	CDKN1B	CDKN2A
CDKN2B	CDKN2C	CHEK1	CHEK2	CIC	CIITA	CREBBP	CSMD3	CTCF	CTLA4
CUL3	CUL4A	CUL4B	CYLD	CYP2C9	CYP2D6	DAXX	DDX3X	DICER1	DNMT3A
DOCK3	DPYD	DSC1	DSC3	ELF3	ENO1	EP300	EPCAM	EPHA2	ERAP1
ERAP2	ERCC2	ERCC4	ERCC5	ERRFI1	ETV6	FANCA	FANCC	FANCD2	FANCE
FANCF	FANCG	FANCI	FANCL	FANCM	FAS	FAT1	FBXW7	FUBP1	GATA3
GNA13	GPS2	HDAC2	HDAC9	HLA-A	HLA-B	HNF1A	ID3	INPP4B	JAK1
JAK2	JAK3	KDM5C	KDM6A	KEAP1	KLHL13	KMT2A	KMT2B	KMT2C	KMT2D
LARP4B	LATS1	LATS2	MAP2K4	MAP2K7	MAP3K1	MAP3K4	MAPK8	MEN1	MGA
MLH1	MLH3	MRE11	MSH2	MSH3	MSH6	MTAP	MTUS2	MUTYH	NBN
NCOR1	NF1	NF2	NOTCH1	NOTCH2	NOTCH3	NOTCH4	PALB2	PARP1	PARP2
PARP3	PARP4	PBRM1	PDCD1	PDCD1LG2	PDIA3	PGD	PHF6	PIK3R1	PMS1
PMS2	POLD1	POLE	POT1	PPM1D	PPP2R2A	PRDM1	PRDM9	PRKAR1A	PSMB10
PSMB8	PSMB9	PTCH1	PTEN	PTPRT	RAD50	RAD51	RAD51B	RAD51C	RAD51D
RAD52	RAD54L	RASA1	RASA2	RB1	RBM10	RECQL4	RNASEH2A	RNASEH2B	RNASEH2C
RNF43	RPA1	RPL22	RPL5	RUNX1	RUNX1T1	SDHA	SDHB	SDHC	SDHD
SETD2	SLX4	SMAD2	SMAD4	SMARCA4	SMARCB1	SOCS1	SOX9	SPEN	STAG2
STAT1	STK11	SUFU	TAP1	TAP2	TBX3	TCF7L2	TET2	TGFBR2	TMEM132D
TNFAIP3	TNFRSF14	TP53	TP63	TPP2	TSC1	TSC2	UGT1A1	USP9X	VHL
WT1	XRCC2	XRCC3	ZBTB20	ZFHX3	ZMYM3	ZRSR2			

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Hotspot mutations (n=165)

ABL1	ABL2	ACVR1	AKT1	AKT2	AKT3	ALK	AR	ARAF	ATP1A1
AURKA	AURKC	AXL	BCL2	BCL2L12	BCL6	BCR	BMP5	BRAF	BTK
CACNA1D	CARD11	CBL	CCND1	CCND2	CCND3	CCNE1	CD79B	CDK4	CDK6
CHD4	CSF1R	CTNNB1	CUL1	CYSLTR2	DDR2	DGCR8	DROSHA	E2F1	EGFR
EIF1AX	EPAS1	ERBB2	ERBB3	ERBB4	ESR1	EZH2	FAM135B	FGF7	FGFR1
FGFR2	FGFR3	FGFR4	FLT3	FLT4	FOXA1	FOXL2	FOXO1	GATA2	GLI1
GNA11	GNAQ	GNAS	H3F3A	H3F3B	HIF1A	HIST1H2BD	HIST1H3B	HRAS	IDH1
IDH2	IKBKB	IL6ST	IL7R	IRF4	IRS4	KDR	KIT	KLF4	KLF5
KNSTRN	KRAS	MAGOH	MAP2K1	MAP2K2	MAPK1	MAX	MDM4	MECOM	MED12
MEF2B	MET	MITF	MPL	MTOR	MYC	MYCN	MYD88	MYOD1	NFE2L2
NRAS	NSD2	NT5C2	NTRK1	NTRK2	NTRK3	NUP93	PAX5	PCBP1	PDGFRA
PDGFRB	PIK3C2B	PIK3CA	PIK3CB	PIK3CD	PIK3CG	PIK3R2	PIM1	PLCG1	PPP2R1A
PPP6C	PRKACA	PTPN11	PTPRD	PXDNL	RAC1	RAF1	RARA	RET	RGS7
RHEB	RHOA	RICTOR	RIT1	ROS1	RPL10	SETBP1	SF3B1	SIX1	SIX2
SLCO1B3	SMC1A	SMO	SNCAIP	SOS1	SOX2	SPOP	SRC	SRSF2	STAT3
STAT5B	STAT6	TAF1	TERT	TGFBR1	TOP1	TPMT	TRRAP	TSHR	U2AF1
USP8	WAS	XPO1	ZNF217	ZNF429					

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CNV Gain (n=127)

ABCB1	ABL1	ABL2	AKT1	AKT2	AKT3	ALK	AR	ARAF	AURKA
AURKC	AXL	BCL2	BCL2L12	BCL6	BRAF	CARD11	CBL	CCND1	CCND2
CCND3	CCNE1	CDK4	CDK6	CHD4	CTNND2	DDR1	DDR2	EGFR	EIF1AX
EMSY	ERBB2	ERBB3	ERBB4	ESR1	EZH2	FAM135B	FGF19	FGF23	FGF3
FGF4	FGF9	FGFR1	FGFR2	FGFR3	FGFR4	FLT3	FLT4	FOXA1	FYN
GATA2	GLI3	GNAS	H3F3A	H3F3B	IDH2	IGF1R	IKBKB	IL7R	KDR
KIT	KLF5	KRAS	MAGOH	MAP2K1	MAPK1	MAX	MCL1	MDM2	MDM4
MECOM	MEF2B	MET	MITF	MPL	MTOR	MYC	MYCL	MYCN	MYD88
NFE2L2	NRAS	NTRK1	NTRK3	PCBP1	PDGFRA	PDGFRB	PIK3C2B	PIK3CA	PIK3CB
PIK3R2	PIM1	PLCG1	PPP2R1A	PPP6C	PRKACA	PTPN11	PXDNL	RAC1	RAF1
RARA	RET	RHEB	RICTOR	RIT1	ROS1	RPS6KB1	RPTOR	SETBP1	SF3B1
SLCO1B3	SMC1A	SMO	SPOP	SRC	STAT3	STAT6	TERT	TOP1	TPMT
U2AF1	USP8	XPO1	YAP1	YES1	ZNF217	ZNF429			

RNA fusion (n=49)

AKT1	AKT2	AKT3	ALK	AR	BRAF	BRCA1	CDKN2A	EGFR	ERBB2
ERBB4	ERG	ESR1	ETV1	ETV4	ETV5	FGFR1	FGFR2	FGFR3	MAP3K8
MET	MTAP	MYB	MYBL1	NOTCH1	NOTCH2	NOTCH3	NRG1	NTRK1	NTRK2
NTRK3	NUTM1	PIK3CA	PIK3CB	PPARG	PRKACA	PRKACB	RAF1	RARA	RELA
RET	ROS1	RSPO2	RSPO3	STAT6	TERT	TFE3	TFEB	YAP1	

※ This test was developed and its performance characteristics determined by GC Genome. It has not been cleared or approved by the Korean Ministry of Food and Drug Safety (MFDS).

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