GCG Oncomine Pan-Cancer Cell-Free Assay

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-	Institution: Hospital A

INDICATION	Lung Cancer

SUMMARY

	Tier 1	Tier 2	Tier 3
Variant	1	2	0
Gene	EGFR	TP53, ERBB2	-

TEST

Tier 1 : Variants of Strong Clinical Significance 1

No	Gene	DNA	Protein	VAF(%)	Depth(X)	COSMIC ID
1	EGFR	c.2573T>G	p.L858R	23.1	5,070	COSM12429

INTERPRETATION

A variant of c.2573T>G (p.Leu858Arg, L858R) has been identified in the EGFR gene. The L858R variant in the EGFR gene is classified as an oncogenic variant with a gain-of-function mechanism. In Non-Small Cell Lung Cancer, the L858R variant in the EGFR gene is an indication for Dacomitinib, Osimertinib, Gefitinib, Erlotinib, Erlotinib + Ramucirumab, and Afatinib.

Tier 2 : Variants of Potential Clinical Significance 2

No	Gene	DNA	Protein	VAF(%)	Depth(X)	COSMIC ID
1	TP53	c.584T>A	p.I195N	32.2	4,748	COSM44877
2	ERBB2	Amplification	6.7 copy number gain*	.	-	.

INTERPRETATION

* The copy number reported is calculated based on the assumption that the tumor burden is 100%. The actual tumor copy number may be higher depending on the tumor burden in the area indicated on the slide and the tissue used for the test.

A variant of c.584T>A (p.Ile195Asn, I195N) has been found in the TP53 gene. Missense variants in the DNA binding domain site of the TP53 gene are classified as likely oncogenic variants with a likely loss-of-function mechanism. There are currently no approved targeted therapies for this type of cancer.

Amplification has been found in the ERBB2 gene. Amplification in the ERBB2 gene is classified as an oncogenic variant with a gain-of-function mechanism. There are currently no approved targeted therapies for this type of cancer.

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

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Tier 3 : Variants of Unknown Clinical Significance	0					
No	Gene	DNA	Protein	VAF(%)	Depth(X)	COSMIC ID
No variant						

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TEST INFORMATION

1. TEST METHOD

Target Region	52 genes
Tested Panel	Oncomine pan-cancer panel(RUO)
Target Enrichment Method	Amplicon-based assay
Massively Parallel Sequencing	Ion S5
Bioinformatic Pipeline	Oncomine TagSeq Pan-Cancer Liquid Biopsy w2.0
Reference Genome	GRCh37/hg19

2. QC DATA

Median Molecular Coverage	5156	Uniformity(%)	96.32
cfDNA Conc.(ng/ul)	11.2	Oncomine / Customized Panel LOD(%)	0.14/0.16

3. LIMITATIONS

- This test was performed using DNA sequencing analysis, and it is possible to detect single nucleotide variant (SNV), small indel, copy number variation (CNV), gene rearrangement in the region included in the test. However it's not possible to detect any variants in the region not covered by the test.
- The detection limit of SNV and small-indel depends on the amount of DNA in the extracted sample and limit of detection (LOD) is about 0.1~2.0% depending on the concentration of cfDNA. And when the tumor proportion is low, variants may not be detected, so clinical correlaton is recommended.
- The four genes (APC, FBXW7, PTEN, TP53) corresponding to tumor suppressor genes among the selected genes included in this test do not cover the entire gene region, but include most of the major pathogenic variants.
- This test does not distinguish germline and somatic variations. If the variant allele frequency of the mutation is close to 50% or 100% in the gene associated with hereditary cancer syndrome, there is a possibility of germline mutation.
- The variants detected in this test are classified into four stages (tier 1 to 4) according to the 2017 JMD guideline (J Mol Diagn 2017; 19:313-327), and tier 4 variations are not reported.

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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

Hotspot genes (n=40)									
AKT1	ALK	AR	ARAF	BRAF	CHEK2	CTNNB1	DDR2	EGFR	ERBB2
ERBB3	ESR1	FGFR1	FGFR2	FGFR3	FGFR4	FLT3	GNA11	GNAQ	GNAS
HRAS	IDH1	IDH2	KIT	KRAS	MAP2K1	MAP2K2	MET	MTOR	NRAS
NTRK1	NTRK3	PDGFRA	PIK3CA	RAF1	RET	ROS1	SF3B1	SMAD4	SMO
Tumor suppressor genes (n=4)									
APC	FBXW7	PTEN	TP53						
Copy number gain genes (n=12)									
CCND1	CCND2	CCND3	CDK4	CDK6	EGFR	ERBB2	FGFR1	FGFR2	FGFR3
MET	MYC								
Fusion genes (n=12)									
ALK	BRAF	ERG	ETV1	FGFR1	FGFR2	FGFR3	MET	NTRK1	NTRK3
RET	ROS1								

※ 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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