Patient Information

LUCENCE DIAGNOSTICS

Name	DOB
JANE TAN	01/03/1973

PATIENT

JANE TAN
Age: 45 Sex: Female
DOB: 01/03/1973
MRN:
Citizen ID: NNNN
Ethnicity: Chinese

PHYSICIAN

YYY YYYY
Order ID: NNNNN
Account ID: NN
Copied to:

SAMPLE

LUCENCE ID: BS-18-NNNNN
Date of Report: DD/MM/YYYY
Date Collected: DD/MM/YYYY
Date Received: DD/MM/YYYY
Type: Blood in Streck tubes (22 mL)

Test Summary

TEST(S) PERFORMED

LiquidHALLMARK®

GENES EVALUATED*
AKT1, ALK, APC, AR, BRAF, CDKN2A, CTNNB1, EGFR, ERBB2 (HER2), ESR1, GNAS, KIT, KRAS, MED12, MET, NRAS, PIK3CA, PTEN, SMAD4, TP53, VHL

MICROSATELLITE LOCI
BAT25, BAT26, NR21, NR24, NR27, MONO27

VIRAL TARGETS
EBV *Bam*HI-W, EBV *EBNA1*

**Targeted regions selected to maximize detection of known hotspot mutations.*

CLINICAL DIAGNOSIS

EGFR MUTANT METASTATIC LUNG ADENOCARCINOMA

TREATMENT HISTORY

FIRST LINE: AFATINIB
SECOND LINE: OSIMERTINIB
THIRD LINE: CHEMOTHERAPY
FOURTH LINE: OSIMERTINIB AND CRIZOTINIB

ABOUT THE TEST

The LiquidHALLMARK® assay is a next-generation sequencing (NGS) based test that identifies targeted somatic genomic alterations and cancer-associated viral DNA in cell-free DNA (cfDNA).

RESULTS SUMMARY

2 Clinically Relevant Genomic Alterations Identified
- EGFR L858R
- MET amplification (2.5-fold)

3 Other Genomic Alteration Identified
- MET R992I
- SMAD4 R441C
- TP53 R65*

Other Actionable Target Genes with No Alterations in Patient Sample
- *KRAS*
- *NRAS*
- *BRAF*
- *ERBB2*
- *PIK3CA*

Other Findings
No detected microsatellite instability at tested markers. No other mutations detected in tested genes.

Clinical Interpretation and Recommendations

CLINICALLY RELEVANT ALTERATIONS IDENTIFIED

Gene	Transcript	Exon	Alteration	Variant Type	Significance	% cfDNA/fold-amplification
EGFR	NM_005228.3	21	c.2573T>G p.L858R (p.Leu858Arg)	Missense substitution	Gain-of-function	4.10%
MET	NM_001127500.2	-	Amplification	-	Gain-of-function	2.5-fold

OTHER GENOMIC ALTERATIONS IDENTIFIED

Gene	Transcript	Exon	Alteration	Variant Type	Significance	% cfDNA
MET	NM_001127500.2	14	c.2975G>T p.R992I (p.Arg992Ile)	Missense substitution	Predicted Splicing variant, Exon skipping	0.35%
SMAD4	NM_005359.5	11	c.1321C>T p.R441C (p.Arg441Cys)	Missense substitution	Likely loss-of-function	0.83%
TP53	NM_000546.5	4	c.193A>T p.R65* (p.Arg65Ter)	Stop gain	Loss-of-function	10.8%

The percentage, or allele frequency, of altered cell-free DNA (% cfDNA) is related to the unique tumour biology of the patient. Several factors may affect the percentages of detected genomic alterations in cfDNA including tumor growth, turnover, size, heterogeneity, vascularization, disease progression or treatment.

INTERPRETATION OF CLINICALLY RELEVANT ALTERATIONS

Variant	Interpretation
EGFR NM_005228.3 c.2573T>G p.L858R (p.Leu858Arg)	EGFR L858R mutation is one of the most common EGFR mutations in NSCLC (26-40%), and the most common sensitizing mutation to EGFR tyrosine kinase inhibitors. EGFR L858R occurs either as a somatic variant, predominantly in non-small cell lung cancer and lung adenocarcinoma. Gefitinib, erlotinib and afatinib are FDA-approved EGFR TKIs for first-line treatment of metastatic NSCLC with EGFR exon 19 deletions or exon 21 (L858R) substitution mutations.
MET amplification	*MET* amplification, *MET* mutations, or aberrant c-MET signaling are associated with unfavorable prognosis in NSCLC. *MET* amplification as a primary driver of tumorigenesis is relatively rare, occurring in only 2% of lung adenocarcinomas, but it can occur in up to 15-20% of *EGFR*-mutant NSCLCs with acquired resistance to EGFR inhibitors, including osimertinib. *MET* amplification is independent of the occurrence of EGFR T790M, and has also been identified in EGFR inhibitor-naive samples. Both *MET* amplification and exon 14 splice mutations have been associated with clinical responses to MET inhibitors. Crizotinib and cabozantinib are two multi-tyrosine kinase inhibitors (MET/ROS1/ALK inhibitors) that have been approved for metastatic NSCLCs with ALK/ROS, and RET rearrangements, respectively. Multiple combinations of MET inhibition and EGFR inhibition have been reported to result in clinical response in case reports or small clinical studies.