THIS IS A DRAFT REPORT.

Patient Details

Name	: XXXXX Srivastav	**Sex / Age**	: F / 57 Years	**Case ID**	: 30503200688
Ref By	: XXXXXX Verma	**Test Name**	: Epitome (HPE+IHC+PDL1+ NGS+ MSI)	**Bill. Loc.**	:

Sample Details

Registration Date & Time	: 2023-05-05 15:11:57	**Sample Type**	: FFPE: XXXX	**Report Date & Time**	: 2023-08-03 04:22:29 PM

Executive Summary

- HPE: Adenocarcinoma of lung
- The tumor cells show immunoexpression of TTF1.
- PDL1 companion diagnostic assay with 22C3 clone shows positive expression of TPS : 55%.
- MSI status by NGS show Microsatelite stable (MSS)
- NGS analysis of the tumor revealed EGFR (Exon 19 deletion) and PIK3CA gene

NGS Report

SNVs

Gene	Variant Nomenclature	Location	Tier	Sensitivity
EGFR (NM_005228.5) VAF: 13.89%	c.2235_2248delinsATTCC p.Glu746_Ala750delinsPhePro	Exon 19	1A	●

● In Disease of Interest ○ In Other Diseases ◐ In Disease of Interest and Other Diseases UF Unfavorable F Favorable NA Not Available

Description

EGFR, a receptor tyrosine kinase, is altered by amplification and/or mutation in lung and brain cancers among others.
The EGFR E746_A750delinsFP alteration has been identified as a statistically significant hotspot and is likely to be oncogenic.
TheEGFR tyrosine kinase inhibitors **osimertinib, dacomitinib, afatinib, erlotinib, and gefitinib are FDA-approved** for the treatment of patients with non-small cell lung cancer harboring an EGFR exon 19 deletion such as E746_A750delinsFP.

Neuberg Oncopath
Unit number 8, Ground Floor,Neelkanth Business park, Nathani Road, Vidyavihar (west), Mumbai. | Phone: 02269396939
Email: info@neubergoncopath.com

NGS Report

Gene	Variant Nomenclature	Location	Tier	Sensitivity
PIK3CA (NM_006218.4) VAF: 33.82%	c.3131A>G p.Asn1044Ser	Exon 21	2C	○

● In Disease of Interest ○ In Other Diseases ◐ In Disease of Interest and Other Diseases UF Unfavorable F Favorable NA Not Available

Description

PIK3CA, the catalytic subunit of PI3-kinase, is frequently mutated in a diverse range of cancers including breast, endometrial and cervical cancers. The PIK3CA N1044S mutation has been identified as a statistically significant hotspot and is likely to be oncogenic. Laboratory data suggest that cancer cells with the PIK3CA N1044S mutation **may be sensitive to the PIK3CA mutant- and isoform-selective inhibitor RLY-2608.**

Technical Notes of NGS (206 genes + MSI)

AMP/ASCO/CAP Classification

Tier I: Variants of Strong Clinical Significance	**1A**	Biomarkers that predict response or resistance to US FDA-approved therapies for a specific type of tumor or have been included in **professional guidelines** as **therapeutic, diagnostic, and/or prognostic biomarkers** for specific types of tumors.
	1B	Biomarkers that predict response or resistance to a therapy based on well-powered studies with consensus from experts in the field, or have diagnostic and/or prognostic significance of certain diseases based on **well- powered studies with expert consensus.**
Tier II: Variants of Potential Clinical Significance	**2C**	Biomarkers that predict response or resistance to therapies approved by FDA or professional societies **for a different tumor type (ie, off-label use of a drug)**, serve as inclusion criteria for clinical trials, or have diagnostic and/or prognostic significance based on the results of multiple small studies;
	2D	Biomarkers that show plausible therapeutic significance based on preclinical studies, or may assist disease diagnosis and/or prognosis themselves or along with other biomarkers based on **small studies or multiple case reports** with no consensus
Tier III: Variants of 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 IV: Benign or Likely Benign Variants		Observed at significant allele frequency in the general or specific subpopulation databases

Methodology :

Massively Parallel Sequencing (Next Generation Sequencing). Tumor Nucleic acid from the submitted specimen was enriched for the coding regions of genes in the panel and splice site junctions of genes. Paired End Sequencing was performed on Illumina platform **(NovaSeq 6000/NextSeq2000)**. Oncocept solid Panel enables the detection of variants in **206 key solid tumor genes.** These genes are well characterized in the published literature and associated with oncology drugs that are FDA approved, part of National Comprehensive Cancer Network (NCCN) guidelines, or in clinical trials. The assay allows concurrent analysis of **DNA and RNA**. Assay

Neuberg Oncopath
Unit number 8, Ground Floor,Neelkanth Business park, Nathani Road, Vidyavihar (west), Mumbai. | Phone: 02269396939
Email: info@neubergoncopath.com

Technical Notes of NGS (206 genes + MSI)

detect multiple types of variants, including hotspots, single nucleotide variants **(SNVs), indels, CNVs, and gene fusions,** in a single workflow.

ABL1	ATRX	CD274	DDR2	EWSR1	FLT3	HRAS	MDM2	MYCN	PALB2	POLE	RB1	SMARCA4	TFEB
ACVR1	BAP1	CD74	DDX3X	EZHIP	FLT4	IDH1	MDM4	MYH7	PAX3	PPARG	RELA	SMARCB1	TMPRSS2
AKT1	BARD1	CDH1	DICER1	FANCA	FOXL2	IDH2	MEN1	NAB2	PAX7	PPP2R2A	RET	SMARCE1	TOE1
AKT2	BCL2	CDK12	DNAJB1	FANCI	FOXO1	JAG1	MET	NBN	PAX8	PRDM6	RHEB	SMO	TP53
AKT3	BCL6	CDK4	DPYD	FANCL	FOXR2	JAZF1	MGMT	NCOA2	PDGFB	PRKCA	RICTOR	SS18	TPM3
ALK	BCOR	CDK6	EGFR	FBXW7	FUS	KDM6A	MLH1	NF1	PDGFRA	PTCH1	ROS1	SSX1	TRAF7
APC	BCR	CDKN1B	EML4	FEV	GLI2	KDR	MN1	NF2	PDGFRB	PTEN	SDC4	SSX2	TSC1
AR	BRAF	CDKN2A	EP300	FGFR1	GNA11	KIF5B	MRE11	NOTCH1	PGR	QKI	SDCCAG8	SSX2B	TSC2
ARAF	BRCA1	CDKN2B	EPCAM	FGFR2	GNAQ	KIT	MSH2	NOTCH2	PIK3CA	RAD51	SDHA	STAT6	VHL
ARID1A	BRCA2	CHEK1	ERBB2	FGFR3	GNAS	KLF4	MSH6	NRAS	PIK3R1	RAD51B	SDHB	STK11	WT1
ASPSCR1	BRIP1	CHEK2	ERBB3	FGFR4	H3-3A	KMT2A	MTOR	NRG1	PKD1	RAD51C	SDHC	SUFU	YAP1
ATF1	CCND1	CREB3L1	ERCC2	FH	H3C2	KRAS	MUTYH	NTRK1	PKHD1	RAD51D	SDHD	SUZ12	YWHAE
ATM	CCND2	CTNNB1	ERG	FLCN	H3C3	MAML2	MYB	NTRK2	PLCB4	RAD54L	SF3B1	TERT	
ATP7B	CCND3	CYSLTR2	ESR1	FLI1	HEY1	MAP2K1	MYC	NTRK3	PMS2	RAF1	SLC34A2	TEX12	
ATR	CCNE1	DDIT3	ETV6	FLT1	HFE	MAP2K2	MYCL	NUTM1	POLD1	RARA	SMAD4	TFE3	

Histopath report (HPE+IHC+PDL1)

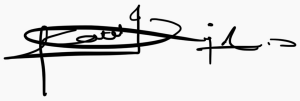
HPE:The core biopsy from the right upper lobe lung lesion reveals an adenocarcinoma in the form of solid glands & small nests.
The tumor cells are cuboidal, have ovoid nuclei with fine chromatin, prominent nucleoli & moderate amount of eosinophilic cytoplasm.
A large proportion of the tumor cells show the presence of intracytoplasmic carminophilic mucin, imparting a signet ring appearance.
Immunohistochemistry was carried out on paraffin block no. (XXXX/23-A).
The tumor cells express CK 7 & TTF-1 and are immunonegative for CK 20.
Impression : CT guided core biopsy from right upper lobe lung lesion:- Poorly differentiated adenocarcinoma of lung.
PDL1 Report
Microscopic Appearance : PDL-1: Tumor proportion score (TPS): 55 %.
Impression : Adenocarcinoma of lung:- PDL-1: Positive with high TPS of 55%.
Comment : The specimen submitted showed adequate viable tumor cells (>100) for PDL1 testing. Positive and negative protein expression controls performed as expected.
Interpretation guidelines:
PD-L1 IHC 22C3 is a qualitative immunohistochemical assay using monoclonal mouse anti-PD-L1, Clone 22C3 intended for use in the detection of PD-L1 protein in formalin-fixed, paraffin-embedded (FFPE) tissues as an aid in identifying patients for treatment with anti PD1/PDL1 inhibitors. This test
has been performed on the Dako AS link 48 platform. PD-L1 protein expression is determined by using either Tumor Proportion Score (TPS) or Combined Positive Score (CPS). The TPS is the percentage of viable tumor cells showing partial or complete membrane staining at any intensity. The specimen is considered programmed death-ligand 1 (PDL1) positive if ≥ 1% of the viable tumor cells exhibit membrane staining at any intensity. If the sample is positive, it is further determined if it is high PD-L1 expression (≥ 50% staining) or low PD-L1 expression (≥ 1% but <50%).
The Combined Positive Score (CPS) is the number of PD-L1 staining cells (tumor cells, lymphocytes, macrophages) divided by the

Neuberg Oncopath
Unit number 8, Ground Floor,Neelkanth Business park, Nathani Road, Vidyavihar (west), Mumbai. | Phone: 02269396939
Email: info@neubergoncopath.com

Histopath report (HPE+IHC+PDL1)

total number of viable tumor cells, multiplied by 100. Although the result of the calculation can exceed 100, the maximum score is defined as CPS 100.

Reviewed By



Dr. Kunjal Patel
MBBS, DNB, PDF (TMC)
Molecular Oncopathologist

Dr. Jay Mehta
MD
Anatomic & Molecular Pathologist

Neuberg Oncopath
Unit number 8, Ground Floor,Neelkanth Business park, Nathani Road, Vidyavihar (west), Mumbai. | Phone: 02269396939
Email: info@neubergoncopath.com