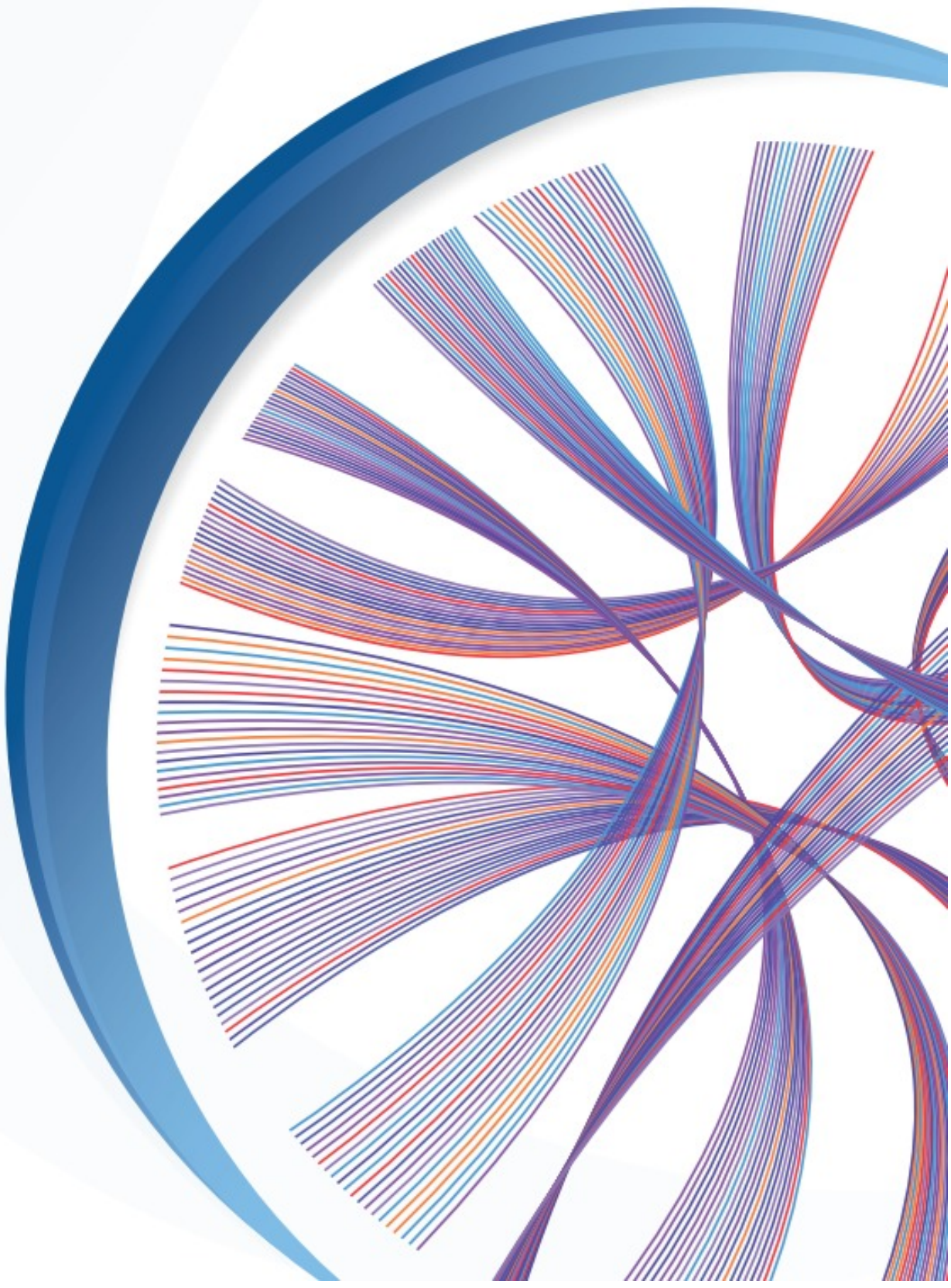
4baseCare
Together, We Beat Cancer

TARGT First

TEST REPORT



PATIENT ID	CANCER SITE	SAMPLE ID	REGISTRATION DATE
IN-423-WCTB	LUNG	IN-423-WCTB-F	20/03/2023

SCOPE OF THE TEST

SNVs, InDels, CNAs, Gene Fusions status

CLINICAL INDICATION

Lung Adenocarcinoma

REPORT DETAILS

Name : NAURANG SINGH

Gender : Male

Age/DOB : 70 Years

Reporting Date : 06/04/2023

Cancer Celltype : Adenocarcinoma, NOS

Sample Source : 130029386

Consulting Clinician : Dr. Amit Jain

Hospital : Valentis Cancer Hospital, Mussoorie Mawana Road

RESULTS

GENOMIC FINDINGS FROM TUMOR PROFILING

Genomic Alteration

EGFR Exon 20(p.His773Leu)
Allelic burden: 18%

Relevant Therapies (in Same Cancer Type)

Therapy	*Clinical Relevance*
NA	NA

Relevant Therapies (in Different Cancer)

Therapy	*Clinical Relevance*	*Cancer Type*
NA	NA	NA

EGFR Exon 20(p.Val774Met)
Allelic burden: 18%

Therapy	*Clinical Relevance*
NA	NA

Therapy	*Clinical Relevance*	*Cancer Type*
NA	NA	NA

**NA: Not Applicable*

STATUS OF VARIANTS IN CANCER RELATED BIOMARKERS

Gene	*BRAF*	*MET*	*KRAS*	*EGFR*	*ERBB2*	*ALK*	*RET*	*ROS1*
Status	Not Detected	Not Detected	Not Detected	**Pathogenic**	Not Detected	Not Detected	Not Detected	Not Detected

Gene	*CDKN2A*	*STK11*	*PIK3CA*	*BRCA2*
Status	Not Detected	Not Detected	Not Detected	Not Detected

GENE FUSION

Gene	*ALK fusion*	*RET fusion*	*ROS1 fusion*
Status	Not Detected	Not Detected	Not Detected

Note:

- The quality of the DNA was suboptimal at the library preparation which probably was due to the intrinsic nature of DNA in this case. However, with the best interest of the patient, the sample was further processed for NGS. Kindly correlate clinically before making any treatment decisions.
- We have identified rare compound mutations (p.Val774Met, p.His773Leu) in exon 20 of the *EGFR* gene. A case report by Chen LC et al., 2019 suggests that compound *EGFR* mutation H773L/V774M was found in a lung adenocarcinoma patient and was found to have poor response to Afatinib, a second generation *EGFR* TKI. Further, a case report by Yang M et al., 2018 suggests that this compound *EGFR* mutation has also been found in another NSCLC patient who demonstrated sustained disease control to osimertinib, though he was unresponsive to the first generation TKI gefitinib. Kindly correlate clinically before making any treatment decisions based on the above findings.

4baseCare Oncosolutions Pvt. Ltd
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PATIENT ID	CANCER SITE	SAMPLE ID	REGISTRATION DATE
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VARIANT DETAILS:

Gene	Variant Location	Variant Consequence	Clinical Significance	Variant Type	Reference
EGFR	chr7:g.55249020A>T, ENST00000275493, Exon 20	c.2318A>T,p.His773Leu , 18%	Pathogenic	Nonsynonymous SNV	ACMG Guidelines
EGFR	chr7:g.55249022G>A, ENST00000275493, Exon 20	c.2320G>A,p.Val774Met , 18%	Pathogenic	Nonsynonymous SNV	rs567477136,VCV000956085.4
IDH1	chr2:g.209113323C>T, ENST00000415913 , Exon 4	c.184G>A, p.Glu62Lys , 47%	VUS	Nonsynonymous SNV	rs144593536, ACMG Guidelines

**NA: Not Applicable*

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TEST DESCRIPTION

TAR**GT** First is a Next Generation Sequencing based test which identifies genetic alterations in a comprehensive panel of well curated 53 tumor genes which can impact response to approved therapy for a particular cancer type. Some of the alterations detected may have bearing on prognosis and/or therapeutic options and may provide relevant information that allows oncologists/clinicians to consider various lines of targeted treatment for the patient.

GENES EVALUATED

TAR**GT** First detects mutations (SNVs and Short Indels), Copy Number Variations (CNVs), gene fusions and splice variants in the 53 genes :

SNVs/InDels Covered in TAR**GT** First

ABL1	*ALK*	*AR*	*ATM*	*BARD1*	*BRAF*	*BRCA1*	*BRCA2*	*BRIP1*	*CDK12*
CDK4	*CDK6*	*CDKN2A*	*CHEK1*	*CHEK2*	*EGFR*	*EPCAM*	*ERBB2*	*ERBB3*	*EZH2*
FANCL	*FGFR3*	*GAPDH*	*IDH1*	*IDH2*	*JAK2*	*KIT*	*KRAS*	*MAP2K1*	*MAP2K2*
MDM2	*MET*	*MLH1*	*MLH3*	*MSH2*	*MSH6*	*NRAS*	*PALB2*	*PDGFRA*	*PDGFRB*
PIK3CA	*PMS1*	*PMS2*	*PPP2R2A*	*RAD51B*	*RAD51C*	*RAD51D*	*RAD54L*	*RET*	*ROS1*
STK11	*TSC1*	*TSC2*							

CNAs Covered in TAR**GT** First

ABL1	*AR*	*ATM*	*BARD1*	*BRCA1*	*BRCA2*	*BRIP1*	*CDK12*	*CDK4*	*CDK6*
CDKN2A	*CHEK1*	*CHEK2*	*EGFR*	*EPCAM*	*ERBB2*	*ERBB3*	*EZH2*	*FANCL*	*FGFR3*
GAPDH	*IDH2*	*JAK2*	*KIT*	*MDM2*	*NRAS*	*PALB2*	*PDGFRA*	*PDGFRB*	*PPP2R2A*
RAD51B	*RAD51C*	*RAD51D*	*RAD54L*	*STK11*	*TSC1*	*TSC2*			

Gene Fusions Covered in TAR**GT** First

ALK	*MET*	*RET*	*ROS1*

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TEST METHODOLOGY

Sample preparation and Library preparation :

DNA isolated from FFPE, or any other fresh tumor tissue source was used to perform targeted gene capture using a custom capture kit. The libraries were sequenced to mean >250X coverage on Illumina sequencing platform.

Bioinformatics Analysis and Reporting :

The sequences obtained are aligned to human reference genome (GRCh37/hg19) and variant analysis was performed using set of Bioinformatics Pipeline. Only non-synonymous and splice site variants found in the panel consisting of specific set of genes were used for clinical interpretation. Silent variations that do not result in any change in amino acid in the coding region are not reported. Clinically relevant mutations were annotated using published variants in literature and a set of databases – ClinVar, COSMIC and dbSNP. Common variants are filtered based on allele frequency in 1000 Genome Phase 3, ExAC, dbSNP, gnomAD, etc. In the absence of a clinically significant reported known variation(s), pathogenicity will be predicted based on in-silico gene prioritization tools: CADD, SIFT, PolyPhen-2, Condel and Mutation taster and prioritized for clinical correlation. The identified pathogenic variant will be correlated with observed phenotypic features of the patient and interpreted according to American College of Medical Genetics (ACMG) guidelines.

Somatic variants are classified into two tiers based on their level of clinical significance in cancer diagnosis, prognosis, and/or therapeutics as per international guidelines: ACMG, ASCO, AMP, CAP, NCCN and ESMO

LIMITATIONS AND DISCLAIMER

- DNA studies do not constitute a definitive test for the selected condition(s) in all individuals. It should be realized that there are possible sources of error. Errors can result from trace contamination, rare technical errors, rare genetic variants that interfere with analysis, recent scientific developments, and alternative classification systems. This test should be one of the many aspects used by the healthcare provider to help with a diagnosis and treatment plan.
- We are using the canonical transcript for clinical reporting which is usually the longest coding transcript with strong/multiple supporting evidence. However, in rare cases, clinically relevant variants annotated in alternate complete coding transcripts could also be reported.
- The contents of this test should be carefully assessed by the treating physician and further interpreted along with clinical, histopathological findings, contraindications and guidelines before deciding the course of therapy.
- The chromosomal aberrations like copy number variations and rearrangements may not be reliably detected with this assay and have to be confirmed by alternate method.
- The sensitivity of this assay to detect large deletions/duplications of more than 10 bp or copy number variations (CNV) is 70-75%. The CNVs detected have to be confirmed by alternate method.
- Most recent block is recommended for testing as the mutation profile may change in response to treatment and hence differ at different sampling points.
- TARGT FIRST test has been developed, validated and performed by 4baseCare Genomics Pvt. Ltd and has not been cleared or approved by the FDA.
- The identified pathogenic variant will be correlated with observed phenotypic features of the patient and interpreted according to (ASCO) guidelines.
- Certain genes may not be covered completely, and few mutations could be missed. A negative result cannot rule out the possibility that the tested tumor sample carries mutations not previously associated with cancer and hence not included in the panel.

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