TARGT LUNG LIQUID ADVANCED

Patient ID: IN-423- XCEAJ **Patient Name: Ms. Rajni Gupta** **Reporting date: 28/03/2024**

Patient Name		**Patient ID**	IN-423-XCEAJ
Gender		**Date of Birth/Age**	67 years
Sample Source		**Sample Collected**	05/03/2024
Referring Clinician			
Hospital			
Clinical Indication			
Scope of the Test			

GENOMIC FINDINGS FROM LIQUID BIOPSY PROFILING

Genomic Alteration	Relevant Therapies (In same cancer type)		Relevant Therapies (In different cancer)		
	Therapy	Clinical Relevance	Therapy	Clinical Relevance	Cancer type
Clinically relevant genomic alterations associated with therapeutic significance were not detected.					

STATUS OF VARIANTS IN CANCER RELATED BIOMARKERS

Gene	*EGFR*	*KRAS*	*BRAF*	*ALK*	*ROS1*	*RET*	*MET*	*ERBB2*	*NTRK1*
Status	**VUS**	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected

Gene	*NTRK2*	*NTRK3*	*NRG1*	*NRG2*	*FGFR2*	*FGFR3*
Status	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected

Gene fusions	*ALK*	*ROS1*	*RET*	*MET*	*NTRK1*	*NTRK2*	*NTRK3*	*FGFR2*	*FGFR3*	*NRG1*	*NRG2*
Status	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected

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Variant details:

Gene	Variant Location	Variant Consequence	Clinical Significance	Variant Type	Reference
EGFR	chr7:g.55238878C>T ENST00000275493 Exon 16	c.1891C>T p.Pro631Ser 44%	VUS	Nonsynonymous SNV	rs552265738 VCV000950603.8 ACMG/AMP Guidelines

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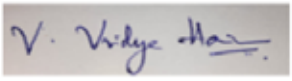
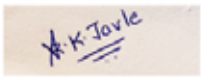


Vidya H. Veldore, PhD
Clinical Director



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TARGT LUNG LIQUID ADVANCED

TEST DESCRIPTION

TARGT Lung Liquid (ADVANCED) is a Next Generation Sequencing based test which identifies genetic alterations in a comprehensive panel of well curated 15 genes which are having an 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

TARGT Lung Liquid (ADVANCED) detects mutations (SNVs and Short Indels), Copy Number Variations (CNVs), gene fusions and splice variants in the 15 genes:

SNVS, SHORT INDELS AND CNVs										
EGFR	*KRAS*	*BRAF*	*ERBB2*	*ALK*	*ROS1*	*RET*	*MET*	*NTRK1*	*NTRK2*	*NTRK3*
NRG1	*NRG2*	*FGFR2*	*FGFR3*							
GENE FUSIONS/SPLICING VARIATIONS										
ALK	*FGFR2*	*FGFR3*	*MET*	*ROS1*	*RET*	*NTRK1*	*NTRK2*	*NTRK3*	*NRG1*	*NRG2*

TEST METHODOLOGY

Sample preparation and Library preparation: Circulating tumor DNA (ctDNA) isolated from plasma, derived from whole blood was used to perform targeted gene capture using a custom capture kit. The libraries were sequenced to mean >1000X 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

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LIMITATIONS AND DISCLAIMERS

- 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 CNVs detected must be confirmed by an alternate method, such as IHC, for further clinical management decisions.
- Our limit of detection for TARGT Lung Liquid (ADVANCED) is 1% for SNVs, 5% for InDels and CNV gain ≥ 6. In addition to this, sequencing quality and coverage is dependent on many factors such as homopolymers, GC-rich regions, intrinsic quality of DNA might impact the variant detection.
- TARGT Lung Liquid (ADVANCED) test has been developed, validated and performed by 4baseCare Oncosolutions 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 sample carries mutations not previously associated with cancer and hence not included in the panel.
- A negative result does not rule out the possibility of mutations in the patient's tumor tissue.