EGFR Liquid Biopsy Test Report

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Patient Information

Patient Name:	M.G.C.R Jayasuriya	**Test**	EGFR Liquid Biopsy Test
Gender:	Male	**Referring Center:**	General Hospital Kandy
Age:	53 Years	**Referred by:**	Dr. Senaka Kandegedara
MRN:	NA	**Sample Collected:**	26-May-2024
Sample ID:	STRAN-2024-51653	**Sample Received:**	29-May-2024
Specimen:	Liquid biopsy	**Report Generated:**	07-June-2024

Overall Result: Negative

Result Summary

Exon	Mutation	Total number of mutations analyzed	Status
18	G719X	3	**Not Detected**
19	Deletion Mutation	29	**Not Detected**
20	Insertion Mutations	6	**Not Detected**
20	T790M	1	**Not Detected**
21	L858R	1	**Not Detected**
21	L861Q	1	**Not Detected**

Interpretation

A positive EGFR mutation test result indicates that the patient's biopsy has a mutation in the EGFR gene. This may make the patient eligible for targeted therapy with EGFR inhibitors, such as erlotinib or osimertinib.

A negative EGFR mutation test result indicates that the patient's biopsy does not have a mutation in the EGFR gene. This does not mean that the patient is not eligible for other treatments, but it does mean that EGFR inhibitors are not likely to be effective.

Background

Alterations in EGFR contribute to the progression and maintenance of the malignant phenotype in non-small cell lung cancer (NSCLC), via gene amplification, overexpression, or mutations. Several clinical studies found that NSCLC tumors harbor mutations in the EGFR gene with a majority of them lying within exons 18 to 21 which maps to the kinase domain of the protein. Hence, EGFR-Tyrosine kinase inhibitors (TKIs) have proven to be effective therapies. The presence of these mutations is associated with increased response to EGFR targeting drugs such as EGFR TKIs. The test is intended to aid in identifying patients with NSCLC that would benefit from anti-EGFR therapy.

Test Attributes

Methodology:

Strand EGFR Liquid Biopsy Test is a lab-developed test (LDT), standardized and validated at Strand Life Sciences. Twenty ml of blood is collected in two Streck tubes (Cell-free DNA BCT, Streck) according to the manufacturer's instructions. The plasma is separated within 48-72 hours and stored at -80°C until further testing. Total circulating DNA is extracted from plasma using Qiagen cfDNA extraction protocol (QIAamp Circulating Nucleic Acid Kit, Qiagen). The level of cell-free DNA is determined. The EGFR test is performed using Super-ARMS EGFR Mutation detection kit (AmoyDx) which is a real time PCR based assay that employs fluorescently labelled probes to qualitatively detect somatic mutations (see Appendix - 1) in exon 18, 19, 20 & 21 of EGFR gene using mutation specific primers.

Analysis:

The analysis is performed using the AriaMX software (Agilent technologies, v.2). Mutant Positive control and NTC are used to establish the threshold for background signal for each dye channel of the assay. The threshold is adjusted to the middle of the highest plateau of Positive control (PC) and the highest background noise of Negative template control (NTC). The Δ ct value is calculated based on the ct value of each mutation present in the sample and results were concluded based on Δ ct cut off values.

Limitations:

This assay is developed, and its performance characteristics are determined by Strand Life Sciences. The sensitivity of the assay is limited where the plasma separation exceeds 48-72 hours. The test results may be influenced by sample integrity and the amount of cfDNA present in the specimen. Therefore, results should be interpreted and correlated with other clinical findings such as clinical histology, stage, and other related information. The EGFR Mutation Test with Super-ARMS EGFR Mutation detection kit is a highly sensitive and specific test, but it is important to note that no test is perfect, false positive and false negative results can occur. Additionally, the test only detects the most common EGFR mutations. There are other, less common EGFR mutations that the test may not detect.

Disclaimer

The test's analytical sensitivity indicates that it can detect mutation when the mutant clone constitutes at least 1% of the total genomic DNA. Although PCR is a highly sensitive technique, contradictory results may arise due to inadequate quality control during sample collection and plasma separation, or the presence of PCR inhibitors. Out of 42 somatic mutations captured by the kit, only 41 mutations are covered by our laboratory testing. Our test does not cover the S7681 2303G>T mutation. The limit of Detection (LOD) of this test ranges from 0.20% to 0.80%.

Compliance Statement:

This test is a Laboratory Developed Test (LDT) and its performance characteristics have been determined by Strand Life Sciences Pvt. Ltd. The test results are for RUO (Research use only) and relate specifically to the sample received in the lab and are presumed to have been collected and transported as per specific instructions given by the physicians/laboratory and belongs to the patient named or identified in the test requisition form.

Recommendations:

a) If the patient has a positive EGFR mutation test result, the healthcare provider should discuss treatment options with the patient. This may include targeted therapy with EGFR inhibitors.

b) If the patient has a negative EGFR mutation test result, the healthcare provider should discuss other treatment options with the patient.

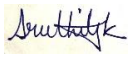
c) Reflex testing with the comprehensive lung cancer panel is recommended for better clinical benefit to patients.

d) Genetic counseling of the patient is recommended.

References

1. Zhang, Z., & Wang, M. (2017). Epidermal growth factor receptor (EGFR) as a therapeutic target in lung cancer. Genes & Diseases, 4(4), 218-225.
2. Sharma, Sreenath V., et al. "Epidermal growth factor receptor mutations in lung cancer." Nature Reviews Cancer 7.3 (2007): 169-181.
3. Huang, Zhen, et al. "The detection of EGFR mutation status in plasma is reproducible and can dynamically predict the efficacy of EGFR-TKI." Thoracic Cancer 3.4 (2012): 334-340.
4. Gazdar, Adi F. "Personalized medicine and inhibition of EGFR signaling in lung cancer." The New England journal of medicine 361.10 (2009): 1018.

Signature



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Supplementary Information

Appendix - 1

Mutation list detected by the assay:

Exon	Mutation	Base Change	Remarks
Exon 18	G719A	2156G>C	It detects 3 mutations but does not distinguish between them.
	G719S	2155G>A	
	G719C	2155G>T	
Exon 19	E746 _A750del (1)	2235 2249de115	It detects 29 mutations but does not distinguish between them.
	E746_A750del (2)	2236 2250de115	
	L747 P753>S	2240 2257de118	
	E746 T751>1	2235_2252>AAT(complex)	
	E746 T751de1	2236 2253de118	
	E746 T751>A	2237 2251de115	
	E746 S752>A	2237 2254de118	
	E746_S752>V	2237 2255>T(complex)	
	E746 S752>D	2238 2255de118	
	L747_A750>P	2238 2248>GC(complex)	
	L747_T751>Q	2238_2252>GCA(complex)	
	L747 E749de1	2239 2247de1TTAAGAGAA	
	L747 T751del	2239 2253de115	
	L747 S752del	2239 2256de118	
	L747_A750>P	2239_2248TTAAGAGAAG>C(complex)	
	L747_P753>Q	2239_2258>CA(complex)	
	L747 T751>S	2240 2251de112	
	L747 T751de1	2240 2254de115	
	L747_T751>P	2239_2251>C(complex)	
	L747 T751de1	2238 2252de115	
	L747 S752>Q	2239 2256>CAA	
	E746 T751>V	2237_2252>T	
	E746_T751>T	2236_2253>ACG	
	L747 A750>P	2239_2250>CCC	
	L747_K754>QL	2239 2261>CAATT	
	E746 K754>EQHL	2238 2261>GCAACATCT	
	E746_S752>EQ	2238 2256>GCAA	
	E746_A750>QP	2236_2248>CAAC	
	E746 T751>Q	2236 2253>CAA	
Exon 20	T790M	2369C>T	
	H773 V774insH	2319 2320insCAC	It detects 6 mutations but does not distinguish between them.
	D770_N771insG	2310 2311insGGT	
	V769 D770insASV	2307 2308insGCCAGCGTG	
	D770_N771insSVD	2311 2312insGCGTGGACA	
	V769 D770insASV	2309 2310AC>CCAGCGTGGAT	
	H773 V774insNPH	2319 2320insAACCCCCAC	
Exon 21	L858R	2573T>G	
	L861Q	2582T>A	

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