MEDGENOME

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DNA TEST REPORT – MEDGENOME LABORATORIES

Patient Name	Santhi B	Gender/Age	F / 55Y
Hospital Name	Cancer Institute (WIA) (Chennai)	Unique Identification Number (UID)	NA
Physician Name	Dr. T.G Sagar	Sample Type	Blood in streck tube
Test requested	*EGFR* T790M mutation screening by ddPCR [MGM548]	Collection Date	NA
		Received date	08-04-2021, 16:50:00
MG Samples ID/ Order ID	594569 / 265932	Report Date	15-04-2021, 23:00:00

RESULTS

T790M mutation (Exon 20) was not detected

CLINICAL CORRELATION AND INTERPRETATION

Epidermal Growth Factor Receptor (*EGFR*) is a cellular transmembrane receptor tyrosine kinase. The activation of *EGFR* plays an important role in tumor growth, proliferation and metastasis. T790M mutation (Exon 20) was not detected in the *EGFR* gene of this subject.

Gene	Mutation	HGVS Nomenclature	Mutation Status
EGFR	Exon 20 (T790M)	c.2369C>T / p.T790M [Chr7:55249071C>T, ENST00000275493]	Not Detected

TEST INFORMATION

Epidermal Growth Factor Receptor (*EGFR*) is a cellular transmembrane receptor tyrosine kinase. The activation of *EGFR* plays an important role in cellular tumor growth and metastasis. *EGFR* tyrosine kinase (TK) gene mutations have been identified in non-small cell lung cancer and patients with *EGFR* mutation positivity are shown to be more sensitive to TK inhibitors [1-3]. Also, during the course of treatment, 60% of the NSCLC patients have been shown to develop T790M resistance mutation, in the Exon 20 of the *EGFR* kinase domain and no longer respond to the first and second generation *EGFR*-TK inhibitors. As per the clinical guidelines (NCCN V2 2016/ESMO 2016), detection of this mutation recommends change of first and second generation TKI to third generation TKI: Osimertinib (Tagrisso), and it has been demonstrated to have improvement in progression free survival in NSCLC [4-7].

The scope of this testing limits to the detection of T790M (Exon 20) in *EGFR* gene. A negative result does not negate absence of *EGFR* mutations that are not covered. Our laboratory established limit of detection for this test is 0.1%.

METHODOLOGY

DNA extracted from the sample is tested for the presence of T790M (Exon 20) of the *EGFR* gene by ddPCR multiplex assay (BioRad Technologies). Droplet Digital PCR is water-oil emulsion technology where the sample is fractionated into 20,000 droplets. The target exon is amplified with mutation specific primers and probe. Once the droplets are generated, PCR is performed and amplification occurs only if the mutation is present at a particular position in the exon, and the mutant amplicons are detected using a novel fluorescent probe. The counting of drops for positive fluorescence values are then used to determine the presence or absence of mutations. Among all the techniques present now, droplet digital PCR remains the most sensitive one which can detect somatic mutations as low as 0.01% [8].

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DISCLAIMER/RECOMMENDATIONS

The results of this test are dependent on the cfDNA yield from the liquid biopsy. Liquid biopsy is a minimally invasive alternative test recommended in NSCLC patients when a tissue biopsy material is insufficient for genotyping or cannot be obtained safely.

- Liquid biopsy is a screening test. It is only a treatment monitoring tool, which could help in assessment of treatment response and early recurrence.
- The results of this test cannot be interpreted without other clinical findings that includes clinical history, imaging and other laboratory analyses.
- A false negative result due to two main reasons:
  - The presence of mutations with low mutant allele fraction below the limit of detection of this assay cannot be ruled out.
  - Could also be due to inherent biology of the tumor, that it did not release enough mutant cell free DNA in circulation. In such cases, it is recommended that a reflex testing on fresh tissue biopsy is performed to decipher the mutation status of *EGFR* gene

REFERENCES

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