Booked on	19/01/2016	**Patient Id**	011601190125	**Printed on**	17/03/2016
Name	Mr. Dheeraj Kumar	**Age**	47 Years	**Sex**	M
Ordering Physician	Dr. Amit Verma				

Somatic Mutations Panel for Cancer (48 genes)

Sample Information

Sample Type: FFPE Tumor tissue

Clinical Indications

Carcinoma; left tongue.

Test Details

48-gene Test - detects somatic alterations in hot spot regions of 48 genes and interprets those with possible therapeutic, clinical or prognostic implications. The test is based on Illumina TruSeq Amplicon Cancer Panel.

Results

Table 1	Genomic alterations that can be targeted with approved drugs						
S.No.	**Gene**	**CDS Variant**	**Amino acid variant**	**Approved drugs against variant**	**Drug Response**	**Hot spot mutation**	**Function of the gene in cancer**
1	KIT	c.1621A>C (ENST00000288135)	p.Met541Leu	Imatinib (Gleevec) Approved in Leukemia and Sarcoma	NA	YES	Oncogene

Table 2	Non- druggable, but clinically altered mutations					
S.No.	**Gene**	**CDS Variant#**	**Amino acid variant**	**Impact on protein Function**	**Function of the gene in cancer**	**Pathway in which the gene functions**

Alignment is performed against the GRCh37/hg19 human genome assembly and annotation is done against the Ensembl release 75 gene model.

cDNA base is reverse compliment of genomic base in case on negative strand.

Test Details & Interpretation

DNA isolated from tumor tissue was used to perform target enrichment and sequencing using tumor gene panel kit which covers clinically significant hotspot coding regions. The tumor tissue was covered at an average sequencing depth of 123X. The sequences obtained were aligned to human reference genome (GRCh37/hg19) using BWA program [2, 3] and analyzed using Picard and GATK-Lite toolkits [4, 5]. Somatic variants were identified and annotated using our in-house annotation pipeline. Clinically relevant mutations were annotated using published variants in literature and a set of well-curated databases including ClinVar, SwissVar, OMIM, GWAS, OncoMD and COSMIC [6-11].

INTERPRETATION:

***KIT*p.Met541Leu (Table 1):**

KIT gene encodes a transmembrane receptor tyrosine kinase (RTK) protein and somatic activating mutations in KIT have been associated with various neoplasms, mainly Gastro-Intestinal Stromal Tumors (GIST). KIT is one of the major targets of imatinib and mutations of KIT gene predict the efficacy of the drug in GIST, melanoma and thymic carcinoma (12). A missense variation (chr4:55593464; c.1621A>C) that results in the amino acid substitution p.Met541Leu was detected in the KIT gene of this subject. This variation is known to confer sensitivity to Imatinib in Leukemia patients (13). The significance of this variation to the patient's cancer type is not known.

Variants of unknown significance (VUS) in genes relevant in cancer

The variants specifically detected in this tumor have not been characterized sufficiently in biochemical assays and therefore their impact in this cancer remains speculative. Two single nucleotide variations (chr4:55972974 T>A; c.1416A>T) and (chr4:55979558 C>T; c.889G>A) that results in amino acid substitutions p.Gln472His and p.Val297Ile receptively were detected in the KDR gene. Kinase insert domain receptor (KDR) promotes the proangiogenic action of vascular endothelial growth factor (VEGF) and is involved in the tumorigenesis and progression of many malignancies. Single-nucleotide variations (SNVs) in KDR have been reported to be associated with the risk and prognosis of several malignancies and are principal targets of anti-angiogenic therapies. SNPs in KDR gene can predict clinical outcome in advanced hepatocellular carcinoma patients receiving first-line sorafenib (14). pVEGFR2/KDR expression is found to be associated with poor prognosis in uveal melanomas and hence inhibitors of this receptor may improve the clinical outcome of patients with pVEGFR2/KDR overexpression (15). However, the variants detected in this subject have not been reported earlier and hence their significance to the patient's cancer type is not known.

Recommendations

Post-test genetic counseling is recommended for the patient and other family members. The physician can request reanalysis of the data, and this is recommended on an annual basis. Data from this test can be reassessed for the presence of any variants that may be newly linked to established genes or to newly identified disorders since the date of this report that could be associated with the patient's phenotype, based on currently available scientific information. A charge may apply for reanalysis.

For further details, kindly contact: contact@molq.in

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******End of the report******

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