RESULTS

Positive Biomarkers:

VARIANT SUMMARY						
Gene	Variant (cDNA Alteration)	Variant (Amino acid Alteration)	Variant Allele Frequency (VAF)	Variant Effect	Variant Classification (AMP)	Variant Classification (ACMG)
EGFR	Exon 19del	p.Glu746_Ala750del	19.60%	GOF	Tier 1	Pathogenic
EGFR	c.2369C>T	p.Thr790Met	4.75%	GOF	Tier 1	Pathogenic

Tier1: variants with strong clinical significance for therapy, prognosis and diagnosis for the same tumor type

RESULT INTERPRETATION AND SUBSEQUENT ACTION

EGFR del 19 or EGFR L858R positive NSCLC patients, who are pre-treated with first and second generation EGFR TKIs generally, develop resistance to the EGFR TKIs by the development of a secondary EGFR T790M mutation. Thus, the co-occurrence of EGFR T790M mutation along with EGFR sensitizing mutations such as EGFR del19 and EGFR L858R mutations confers resistance to first and second generation EGFR TKI therapy (Erlotinib, Gefitinib, or Afatinib) and warrants intervention with agents that specifically target the EGFR T790M mutation. Number of clinical and preclinical studies have reported that Osimertinib, has shown encouraging results in metastatic NSCLC patients harbouring EGFR T790M-mutations. [PMID: 27959700, 29151359].

Several studies suggest T790M can occur at low levels in patients who have not previously received EGFR TKI therapy, which might contribute to predicting recurrence of the tumor in response to the TKI therapies, although this is a rare event [PMID: 21635547, 28989039, 24478319, and 25134330]. Since the VAF of EGFR p.T790M was <5%, and the patient was treatment naïve, digital droplet polymerase chain reaction (ddPCR) was done to confirm the presence of the said variant and sample tested positive for EGFR p.T790M by ddPCR.