RESULTS

Gene	Variant	Variant (Amino acid Alteration)	Variant Allele Frequency (VAF)	Variant Effect$	Variant Classification (AMP)#	Variant Classification (ACMG)!
EGFR	c.2236_2250 delGAATTAA GAGAAGCA	p.Glu746_Ala750del	35.5%	GOF	Tier 1	Pathogenic
EGFR	c.2369C>T	p.Thr790Met	2.75%	GOF	Tier 1	Pathogenic
BRAF	c.1799T>A	p.Val600Glu	5.8%	GOF	Tier 1	Pathogenic

INTERPRETATION :

The patient was found to be positive for three mutations EGFR exon 19 deletion, EGFR T790M and BRAF V600E mutation. No other clinically relevant mutation(s) were detected in the ALK, MET, and ROS1 genes for the index patient.

DISCUSSION:

In 2018, Osimertinib was approved by the Food and Drug Administration for the treatment of epidermal growth factor receptor (EGFR)-mutant lung cancer patients and it is used for patients with acquired T790 M mutations after 1st and/or 2nd generation EGFR tyrosine kinase inhibitor (TKI) treatment, but more recently it began to be used in first line treatment of EGFR-mutant patients. Despite good initial responses, patients developed resistance to second-line osimertinib treatment. For this resistance several mechanisms have been identified, including an acquired v-raf murine sarcoma viral oncogene homolog B1 (BRAF) V600E mutation.

EGFR and BRAF molecular alterations are cancer drivers genes. The above case study presents concurrent alterations in both EGFR and BRAF. Concomitant mutations will definitely have different tumor mutation burden as well as different level of phosphorylation of BRAF and EGFR. Hence, patients would respond differently to targeted therapies than they might have responded in case of single mutation of EGFR or BRAF (figure1). Formal therapeutic guidelines regarding management of such cases with unusual genomic aberrations are not available. Under dabrafenib, trametinib, and osimertinib in an advanced EGFR-mutant lung adenocarcinoma patient who developed BRAF V600E as one of the acquired resistance mechanisms to second-line osimertinib. But combination of dabrafenib, trametinib,