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Abstract Title:- Cell-free DNA-based Next Generation Sequencing LungTrack Advance test to detect actionable gene mutations and fusions in NSCLC patients.

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Aims:-Identifying targetable molecular changes is crucial when determining the appropriate treatment for non-small cell lung cancer (NSCLC) patients. While tissue biopsy (TB) is currently the standard method for assessing genomic alterations, there are situations where obtaining a TB is not feasible due to patient consent issues, limited tissue availability, low tumor content, or challenges in extracting nucleic acids. To address these challenges, liquid biopsy (cell-free DNA)-based sequencing tests are a promising alternative.

Methods:- Here, we present the mutation profiles of 98 NSCLC patients (Treatment Naive (24); Progressed on treatment (74)) using a laboratory-developed, CAP-accredited Next Generation Sequencing (NGS) liquid biopsy test called LungTrack Advance from MedGenome Labs, India. This test accurately detects single nucleotide variants (SNVs), small insertions/deletions (InDels), and gene fusions in actionable genes.

Results:- Among the 24 treatment-naive patients, actionable variants were identified in 45.3% of cases. Specifically, EGFR gene mutations were found in 6 patients, including Exon 19 deletions (3), Exon 20 insertions (1), and L858R mutations (2). Additionally, one patient had a KRAS (G12C) mutation, two patients had ERBB2 mutations, one had a BRAF V600E mutation, and three had gene fusions, including EML4/ALK (1) and CD74/ROS1 (2).

In the 74 patients who had progressed on treatment, 55.4% carried actionable variants, either with or without resistance mutations. EGFR gene mutations were found in 29 patients among other mutations like EML4/ALK fusion (3), ROS1 fusion (4), BRAF V600E (1), MET exon 14 skipping mutation (2), ERBB2 exon 20 ins (3) & RET fusion (1). Among EGFR mutations, T790M resistance mutation was detected in 8 patients in combination in Exon 19 del (5), L858R (2) and alone (1). In a patient with CD74/ROS1 fusion, a resistance mutation G2026R in ROS1 gene was identified. Notably, in a patient with a CD74/ROS1 fusion who had progressed on chemotherapy and had insufficient tissue for a rebiopsy, the LungTrack Advance test identified an EZR/ROS1 fusion. Administering Crizotinib led to a partial response after six months of follow-up.

Conclusions:- This data underscores the significance of NGS-based liquid biopsy testing in NSCLC patients, especially when traditional tissue biopsies are impractical or when re-biopsy is needed for relapsed cases. Liquid biopsy can efficiently detect mutations and fusions, aiding in treatment decision-making.

Keywords:- Cell-free DNA, Liquid Biopsy, NGS, Non-small Cell Lung Cancer, Fusions