128P- Precision genomics based targeted 12 gene biomarker and PD-L1 testing in advanced non-small cell lung cancer patients as an alternative to conventional EGFR, ALK, ROS1 sequential testing in a tertiary care hospital

Madhu Nagaraj, Shekar Patil, Ravi Thippeswamy, Satheesh Chiradoni Thungappa

Department of Medical Oncology, Health Care Global Enterprises (HCG) Ltd. Cancer Hospital, Bengaluru, India

Background

The standard of care in our hospital for advanced non-small cell lung cancer was conventional EGFR, ALK, ROS1 sequential testing and to treat with chemotherapy if no actionable genetic mutations were detected.

With the evolving precision medicine-based new targeted treatments for lung cancer patients, we planned a study to develop a new next-generation sequencing (NGS)-based assay to identify clinically relevant 12 genes most frequently mutated in non-small cell lung cancer to help patients to benefit from precision genomics-based new targeted treatment approaches and to avoid chemotherapy use.

Methods

The study population consisted of **newly diagnosed** or **previously treated advanced non-small cell lung cancer** patients. After analysis of the formalin-fixed paraffin-embedded (FFPE) blocks for tumor content, DNA and mRNA from FFPE blocks were extracted and subjected to 12 gene biomarker testing by next-generation sequencing (NGS) using the Ion S5 system. The test utilizes AmpliSeq technology-based NGS assay. High-quality nucleic acids that passed quality control checks were subjected to the library preparation and analysed for relevant genomic alterations in both the DNA and RNA to simultaneously detect multiple variants including hotspots, single-nucleotide variants (SNVs), indels, copy number variants, and gene fusions as mentioned below.

Hotspot genes (SNVs and short indels): **EGFR, ALK, ROS1, BRAF, ERBB2, KRAS, NRAS, PIK3CA, MET exon 14 skipping mutation, RET, and MAP2K1.**

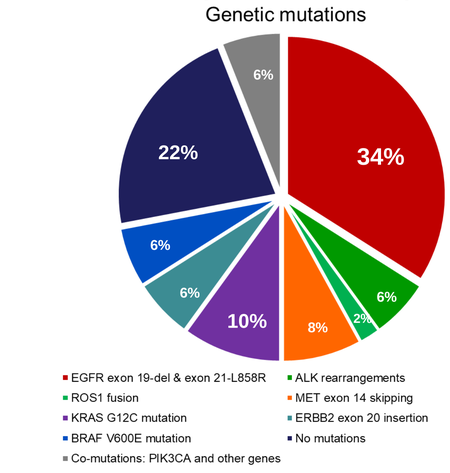
Gene fusions: ALK, ROS1, RET, METΔex14, **NTRK genes 1/2/3**.

Sequencing was performed to achieve a minimum 500x depth of coverage. High-quality sequencing data was then analysed using the optimized Ion torrent suite to accurately detect rare somatic variants. The hotspots, indels, and fusions were analysed with the help of Ion reporter software and variants were annotated according to ACMG and AMP guidelines.

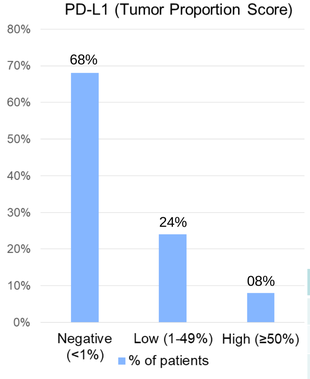
Results

In our study conducted over a period of 6 months, a total of around **50 patients** underwent 12 gene biomarker testing by NGS. The mean age of our study population was 63.3±11.75 years, comprising of 60% males (n=30) and 40% females (n=20). Histopathology report was **adenocarcinoma** in **98%** (n=49) and **squamous cell carcinoma** in **2%** (n=1) of patients. The **mean turnover time** between the analysis of FFPE blocks for tumor content and NGS testing results was **14±2 days** respectively.

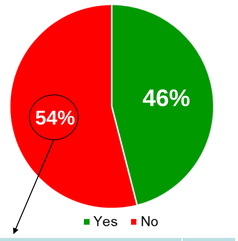
Genetic mutations



PD-L1 (Tumor Proportion Score)



Precision genomics-based targeted treatment



No mutations present	**41%**
Unaffordable drug price	26%
No Indications for targeted therapy	22%
No access to drugs or clinical trials	11%

Conclusion

Our study of precision genomics-based **12 gene biomarker** testing by **next-generation sequencing (NGS)** as an alternative to conventional EGFR, ALK, ROS1 testing in advanced non-small cell lung cancer patients is a **cost-effective** and **time-saving** approach for targeted treatment in a tertiary care hospital.

Legal entity responsible

The authors.

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Disclosures

All authors have declared no conflicts of interest.

For more information please contact the author- drmadhunagaraja@gmail.com