EP06.09-Actionable Genomic Alterations and Co-Mutation Landscape in Metastatic NSCLC: Real-World NGS Data From India

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INTRODUCTION

• Broad-panel NGS is central to treatment selection in metastatic NSCLC.

• Indian real-world data on actionable alterations, rare drivers and co-mutation patterns remain limited.

• Aim: describe the genomic landscape of mNSCLC using a pragmatic ESCAT-aligned framework, including actionable drivers and biologically relevant co-mutations.

METHODS

RETROSPECTIVE REAL-WORLD COHORT

107 — **mNSCLC patients**

Jan 2023-Feb 2026 — **Study period**

NGS — **All patients**

ESCAT — **Pragmatic actionability classification**

Collected: all genomic report fields
Classified: Tier 1 actionable • Tier 2/3 emerging • co-mutations
Analysis: driver frequencies, sex distribution and molecular-subset co-alterations

DISCUSSION AND CONCLUSION

ACTIONABLE TAKE-AWAY

• Tier 1 alterations were found in nearly two-thirds of patients.

• Rare targetable drivers formed a clinically meaningful subset (~15%).

• TP53 dominated the co-mutation landscape; STK11/KEAP1 clustered more often with KRAS.

• Broad-panel NGS may prevent missed treatment opportunities in Indian mNSCLC practice.

FUTURE DIRECTION

Link co-mutation patterns with treatment response, PFS and OS in larger prospective clinicogenomic cohorts, and evaluate whether specific co-alterations refine risk beyond the primary oncogenic driver.

REFERENCES & ACKNOWLEDGEMENTS

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Framework: ESMO Scale for Clinical Actionability of molecular Targets (ESCAT).
Track: Molecular Pathology

RESULTS

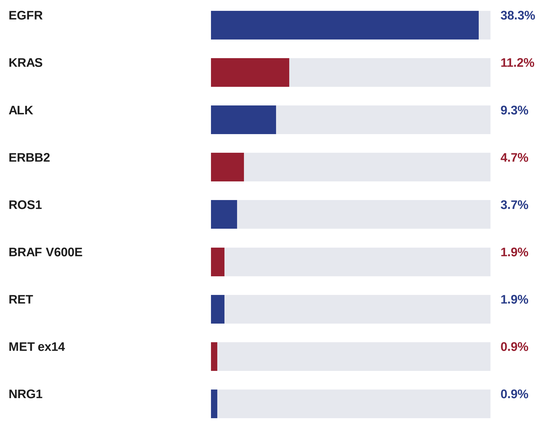
107 patients • 87% adenocarcinoma • median age 64 years • 54 male / 53 female

64.5% — **TIER 1 ACTIONABLE 69 / 107**

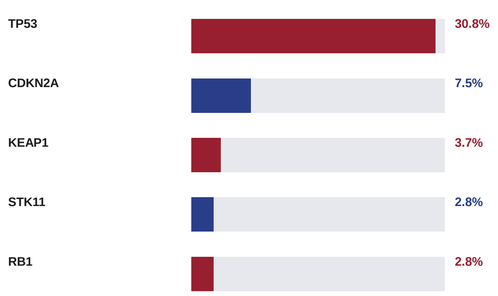
~15% — **RARE TARGETABLE ALTERATIONS**

30.8% — **TP53 CO-ALTERATION**

DRIVER ALTERATION LANDSCAPE



CO-MUTATION LANDSCAPE



TIER 1 ACTIONABILITY BY SEX



RARE BUT TARGETABLE ALTERATIONS

RET fusion • ROS1 fusion • ERBB2
NRG1 fusion • MET exon 14 skipping
BRAF V600E • MSI-H

Together: approximately 15% of the cohort

MOLECULAR SUBSET SIGNALS

KRAS G12C: 3 / 12 KRAS-mutant tumors (25%)

STK11 + KEAP1: enriched in KRAS-mutant tumors
TP53: commonly co-altered with EGFR-mutant disease

WHY THIS MATTERS

Genomic heterogeneity was substantial. Broad-panel NGS identified both common actionable drivers and uncommon therapeutic opportunities that limited sequential testing could miss.