

Distinct co-mutation signatures of KRAS-mutant non-small cell lung cancer define molecular heterogeneity and immunotherapy response in an Asian cohort

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BACKGROUND

- KRAS is mutated in 25–30% of Western but only 10–15% of Asian NSCLC, and G12C predominates in Western series.
- G12C, G12D and G12V differ in biology, co-mutation landscape and clinical phenotype.
- STK11, KEAP1 and TP53 co-alterations modify checkpoint-inhibitor benefit, yet Asian evidence is scarce and largely plasma-based.

OBJECTIVE

To define subtype-specific clinical, genomic and survival characteristics of KRAS-mutant NSCLC — and the influence of co-occurring alterations on immunotherapy outcome — in a Korean multicentre cohort.

METHODS

- Design: retrospective cohort, National Cancer Center and Seoul St. Mary's Hospital; systemic therapy between Jan 2017 and Dec 2023, follow-up through Dec 2024.
- Patients (n = 171): stage IV or recurrent NSCLC with NGS-confirmed KRAS mutation receiving first-line palliative systemic therapy. A further 22 patients (2024–2025) were profiled for genomic comparison only.
- Genomics: ctDNA FoundationACT (n = 111); tissue Oncomine Comprehensive Assay v3 (n = 9) and OCA Plus 501-gene panel (n = 51; VAF ≥ 2%, depth ≥ 500×). TMB was not comparable across platforms and was not analysed.
- PD-L1: SP263 tumour proportion score, available in 151 of 171 patients.
- Statistics: χ^2 / Fisher exact and Mann–Whitney / Kruskal–Wallis tests; Kaplan–Meier with log-rank; Cox proportional hazards; pairwise co-mutation by 2×2 Fisher exact with log₂ odds ratios. SPSS 26, Prism 9, R 4.5.1.

STUDY COHORT

