

Real-World Genomic Landscape and Survival Heterogeneity in an Asian Cohort of NGS-Tested Advanced NSCLC

Ji-Youn Han, Eun Jin Lim, Byngchul Ahn, Youngjoo Lee

National Cancer Center, Goyang, Republic of Korea



Introduction

- Lung cancer remains the leading cause of cancer death worldwide; NSCLC accounts for the majority of cases. Oncogenic driver mutations — EGFR, ALK, ROS1, BRAF, MET, RET, and KRAS — have transformed NSCLC into molecularly defined subtypes with distinct treatment implications.
- NGS enables simultaneous, tissue-sparing interrogation of dozens of genes, capturing alterations that sequential single-gene testing misses — yet real-world survival outcomes across the full AGA spectrum remain insufficiently characterized in Asian populations.
- We aimed to describe the genomic landscape and evaluate OS across molecular subgroups in a large, real-world NGS-tested Asian cohort.



Methods

- Design: Retrospective analysis of 648 patients with advanced NSCLC who underwent NGS at the National Cancer Center of Korea, December 2016–November 2025.
- NGS methods: Tissue NGS was performed using the Oncomine™ Comprehensive Assay v3, while plasma NGS was performed using Guardant360® or FoundationOne® Liquid CDx.
- Analysis: AGA frequencies assessed; OS defined from diagnosis to death/last follow-up, estimated via Kaplan-Meier method with log-rank comparisons across genomic subgroups.

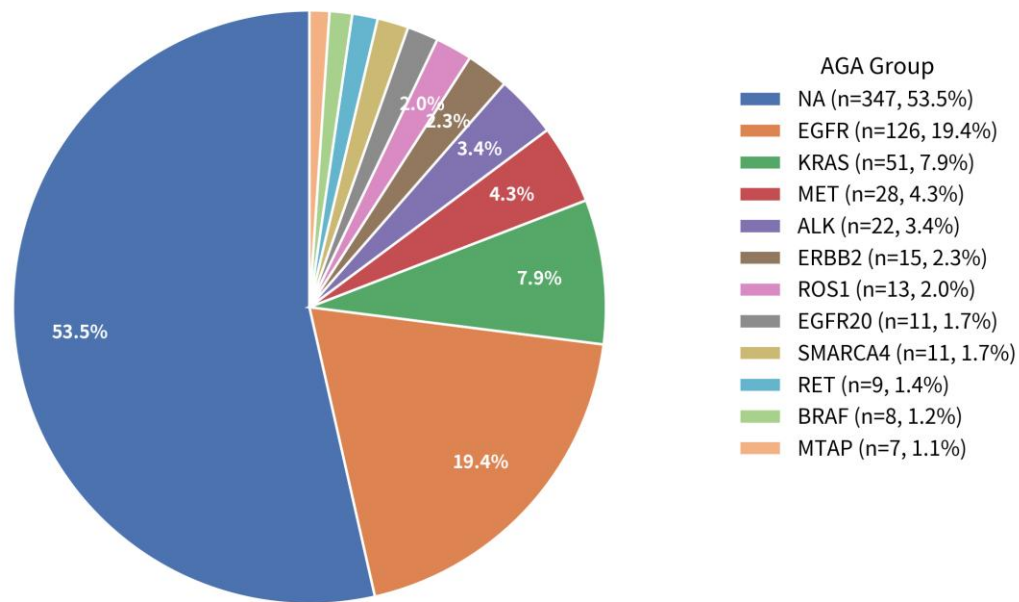
Cohort Demographic Features	
Age, median (range)	69 (19-89)
Gender	
Male	457
Female	191
Stage	
IIIB	38
IV	610
Histology	
Adenocarcinoma	498
Squamous cell carcinoma	79
Large cell neuroendocrine carcinoma	9
pleomorphic carcinoma	26
sarcomatoid carcinoma	14
NOS	22
Smoking	
Never	201
Former	333
Current	114
NGS testing	
Tissue	333
Plasma	315



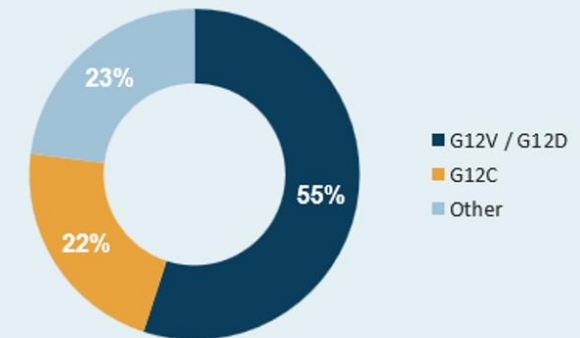
Genomic Landscape

- The most frequent AGAs were EGFR (19.4%) and KRAS (7.9%), followed by MET exon 14 skipping, ALK fusion, and ERBB2.
- A total of 347 patients (53.5%) had no detectable AGA.
- Relatively low EGFR/ALK frequencies reflect pre-screening by non-NGS assays in routine practice.

Distribution of AGA Groups (N = 648)



KRAS G12 Variant Distribution

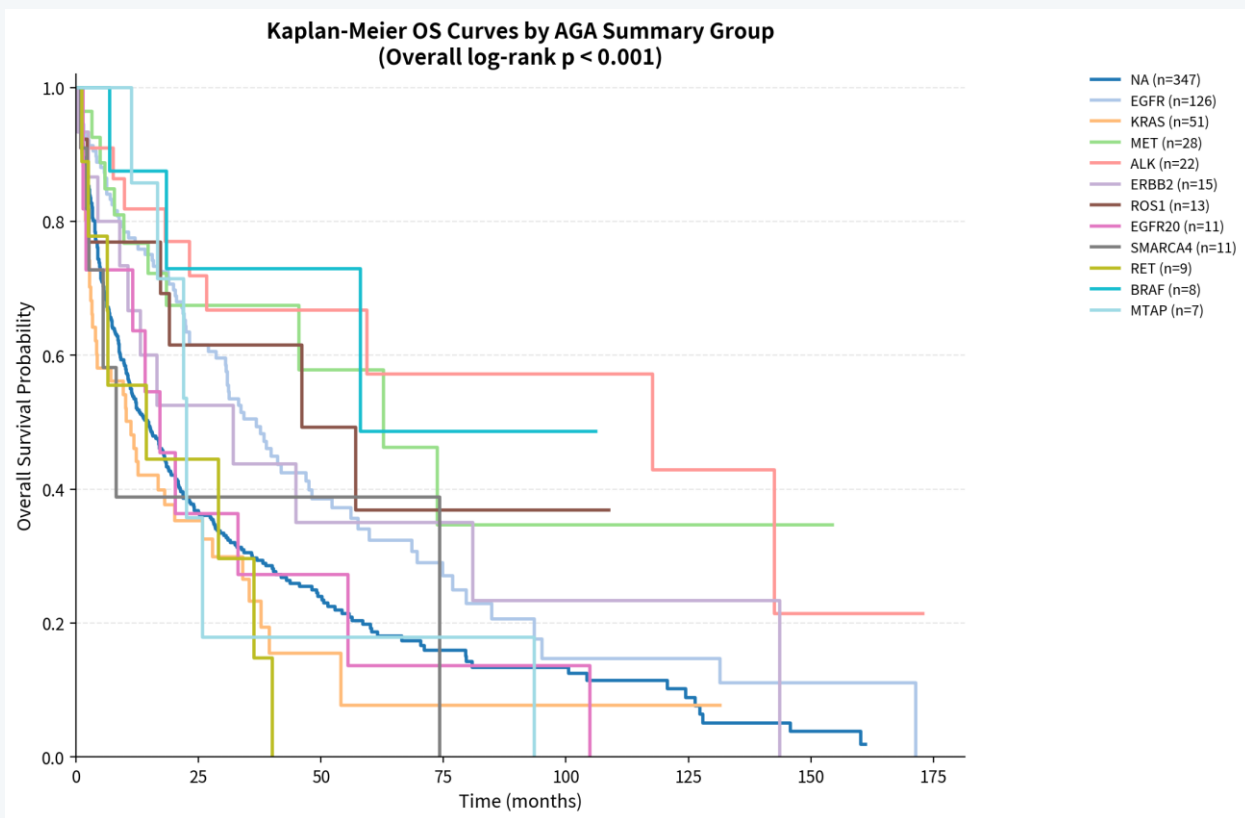


Among KRAS-mutant tumors, non-G12C variants (G12V/G12D, Other) predominate over G12C — a pattern distinct from Western cohorts.



Survival by AGA Subgroups

Median OS varied markedly across genomic subgroups (log-rank $p < 0.0001$), ranging from 8.2 months (SMARCA4) to 117.7 months (ALK).



Median Overall Survival by AGA Summary Group

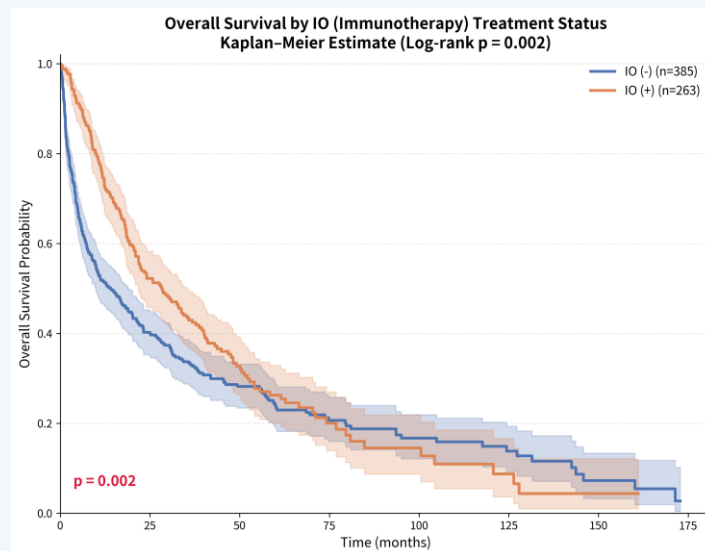
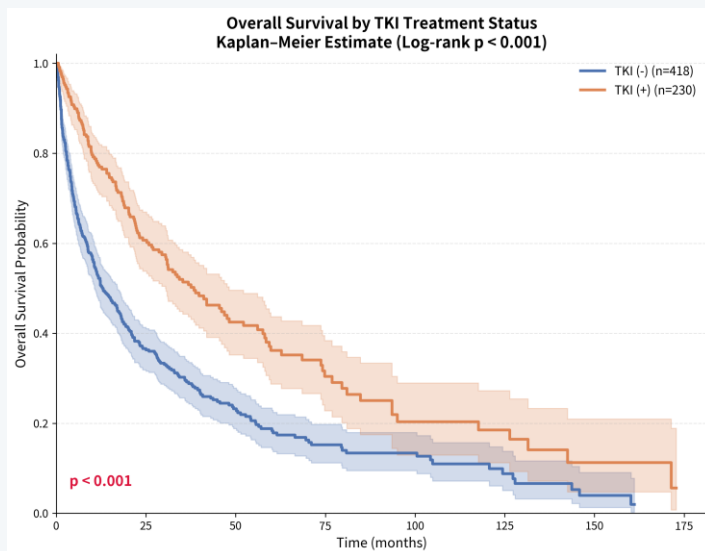
Kaplan-Meier estimates with 95% confidence intervals (Brookmeyer-Crowley method)

AGA Group	N	Events	Median OS (months)	95% CI (months)
NA	347	275	14.8	11.1–18.1
EGFR	126	81	36.8	30.5–47.6
KRAS	51	39	11.2	3.4–20.1
MET	28	11	62.8	18.5–NR
ALK	22	10	117.7	23.1–NR
ERBB2	15	11	32.1	4.4–143.7
ROS1	13	7	46.1	2.3–NR
EGFR20	11	10	17.1	1.4–55.5
SMARCA4	11	6	8.2	2.1–74.2
RET	9	8	14.3	1.2–36.3
BRAF	8	3	58.1	6.8–NR
MTAP	7	6	22.6	11.3–93.6

NR, median not reached due to insufficient number of events.

Impact of Treatment

- Both targeted therapy and immunotherapy were associated with longer OS.
- Immunotherapy was associated with longer OS among patients without detectable AGAs and those harboring KRAS or SMARCA4 alterations.

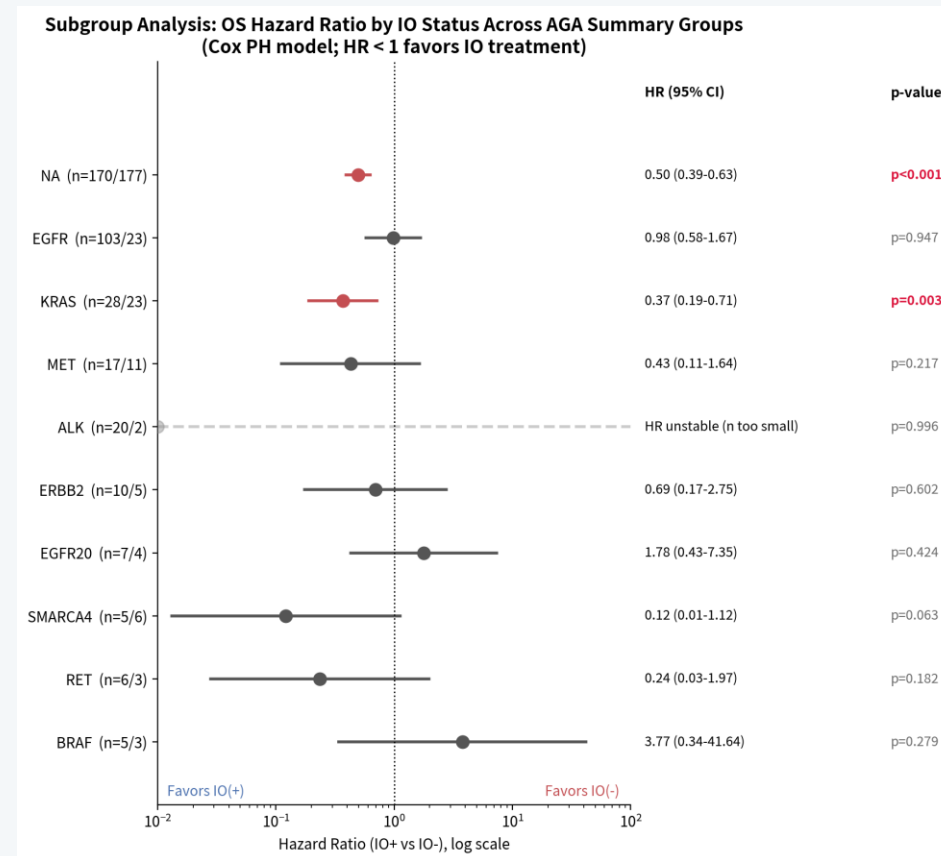


Median Overall Survival by Treatment Status				
Kaplan-Meier estimates with 95% CI (Brookmeyer-Crowley method)				
Treatment	N	Events	Median OS (months)	95% CI (months)
TKI (-)	418	328	12.9	10.6-17.0
TKI (+)	230	139	38.4	30.5-48.2
Log-rank (TKI)				$p < 0.001$
IO (-)	385	287	14.1	9.9-19.1
IO (+)	263	180	28.3	21.8-35.3
Log-rank (IO)				$p = 0.002$



Subgroup Analysis: OS by IO Status Across AGA Groups

Immunotherapy was associated with significantly improved OS in patients with no detectable AGA and in the KRAS subgroup; other subgroups showed wide confidence intervals reflecting small sample sizes.





Conclusions

- Survival in this real-world cohort was strongly associated with the availability and use of effective targeted therapies.
- Patients with ALK fusions and MET exon 14 skipping had particularly favorable outcomes.
- In contrast, RET-, KRAS-, and SMARCA4-altered tumors remained poor-prognosis subsets, further compounded by the predominance of non-G12C KRAS variants in this Asian population.
- Immunotherapy was associated with longer OS among patients without detectable AGAs and those harboring KRAS or SMARCA4 alterations.
- These findings should be interpreted cautiously because of the retrospective design and potential treatment-selection bias.