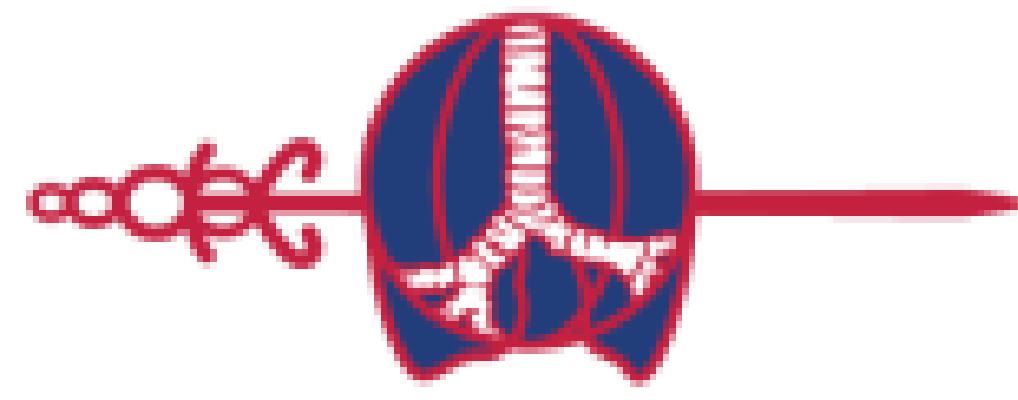




IASLC



2026 World Conference on Lung Cancer



IASLC 2026 World
Conference on Lung Cancer

SEPTEMBER 12 – 15, 2026
SEOUL, REPUBLIC OF KOREA

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EP06.08 - Computational Analysis of Lung Carcinoma Across Early and Advanced Stages

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Why look beyond actionable drivers?

The prognostic meaning of the NSCLC genomic landscape remains incompletely defined.

Current paradigm

Molecular testing is established for treatment selection, particularly in advanced NSCLC. Targeted and immune-based strategies are increasingly moving into earlier disease stages.

Knowledge gap

Most evidence focuses on individual drivers or advanced-stage cohorts. The contribution of co-occurring alterations to recurrence and survival is less clear.

LANTERN question

Can broad genomic profiling—integrated with clinical variables and PD-L1—identify prognostic subgroups across the disease continuum?

AIM

To evaluate individual mutations, pairwise co-mutations and stage-specific genomic–PD-L1 associations in a prospective real-world cohort.



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Study design and analytical workflow

271

consecutive NSCLC
patients

137

stage I–III

134

stage IV

523

cancer-related genes

Tissue

FFPE tumor tissue
≥20% viable tumor
cells

CGP

TruSight Oncology
500 HT
SNVs • indels •
CNVs • TMB • MSI

PD-L1

SP263 IHC
TPS: <1% • 1–49% •
≥50%

Statistics

Stage-adjusted Cox
models
Pairwise co-
mutations
Fisher exact test

Prospective, multicenter, observational
Enrollment → March 2023–December 2024



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A balanced real-world cohort across disease stages

69 y

median age (28–87)

50.2%

male

86.3%

adenocarcinoma

75%

current/former
smokers

229

PD-L1 evaluable

Disease stage

Stage I 35.8%

Stage II–III
14.8%

Stage IV 49.5%

PD-L1 distribution (n=229)

<1% 34.1%

1–49% 28.8%

≥50% 37.1%



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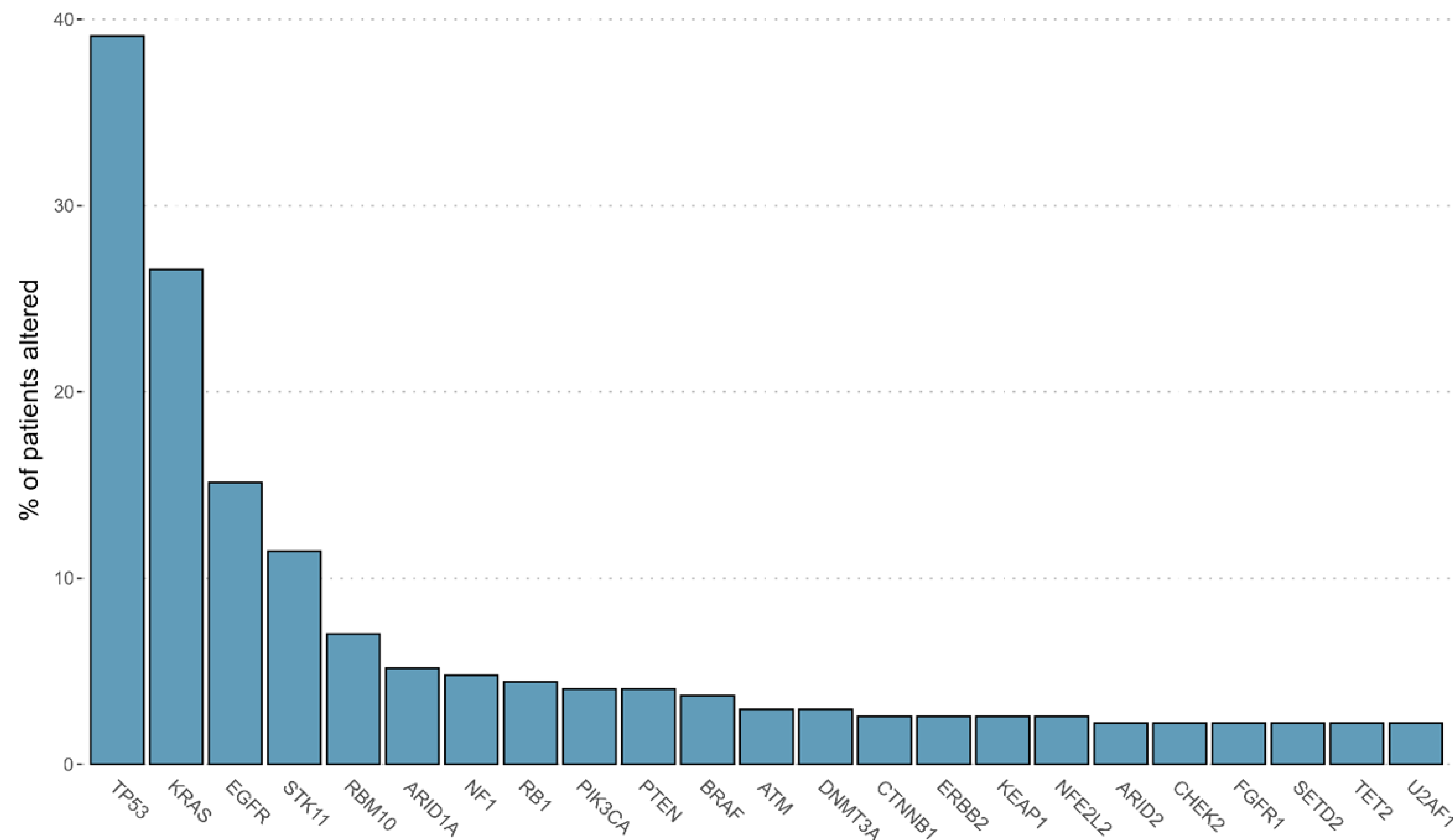
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Broad profiling reveals a heterogeneous genomic landscape

At least one Tier I–II molecular alteration was identified in 84% of patients.

Distribution of most frequently mutated genes



TP53

39% — most frequently altered

KRAS

27% — second most frequent

EGFR / STK11

15% / 11%

Long tail of lower-frequency alterations underscores the value of comprehensive profiling.



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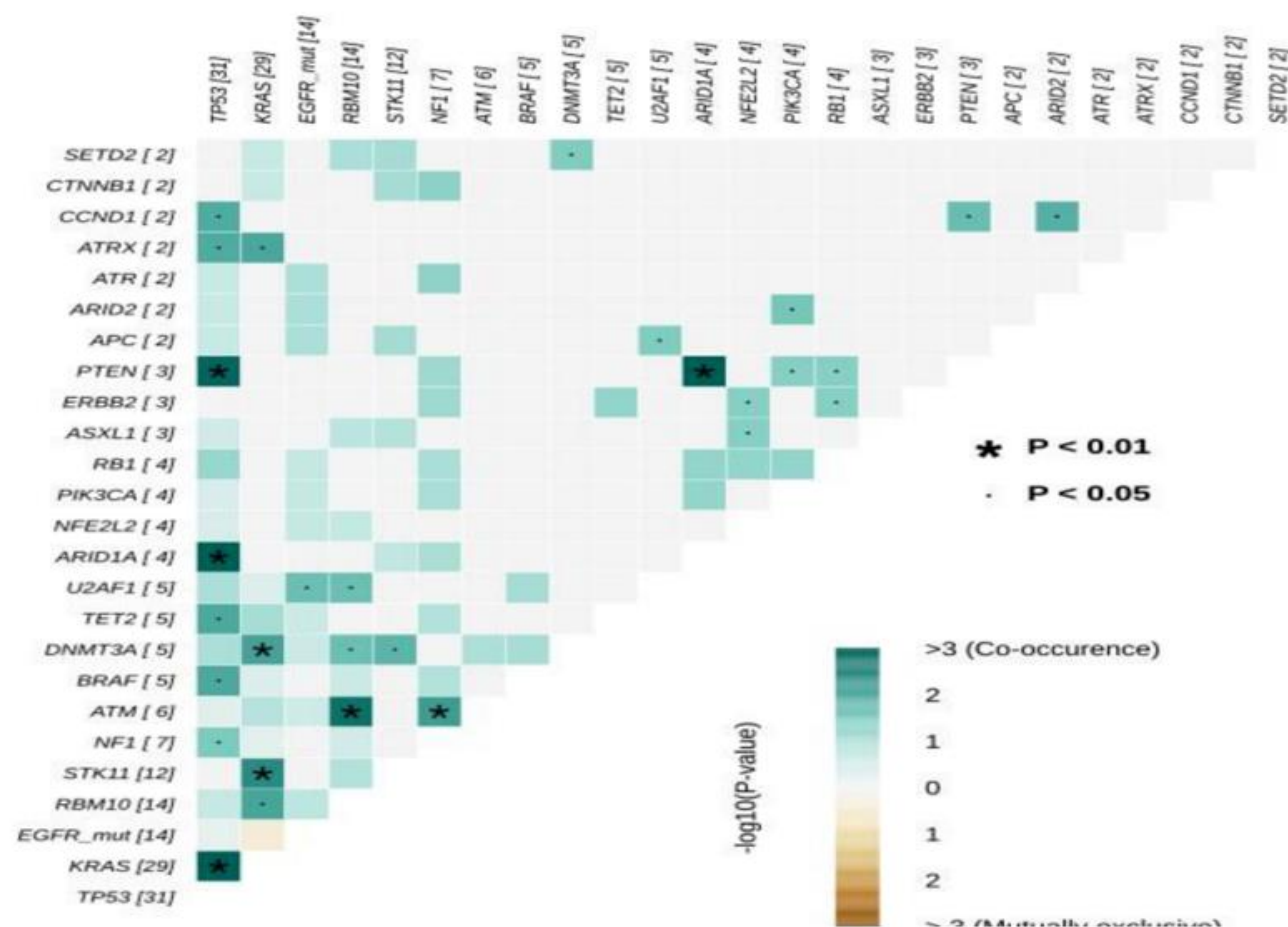


Stage-specific co-mutational architecture

The ELCC 2026 analysis provides a direct visual comparison of genomic interactions across disease stages.

Early / locally advanced (I–III)

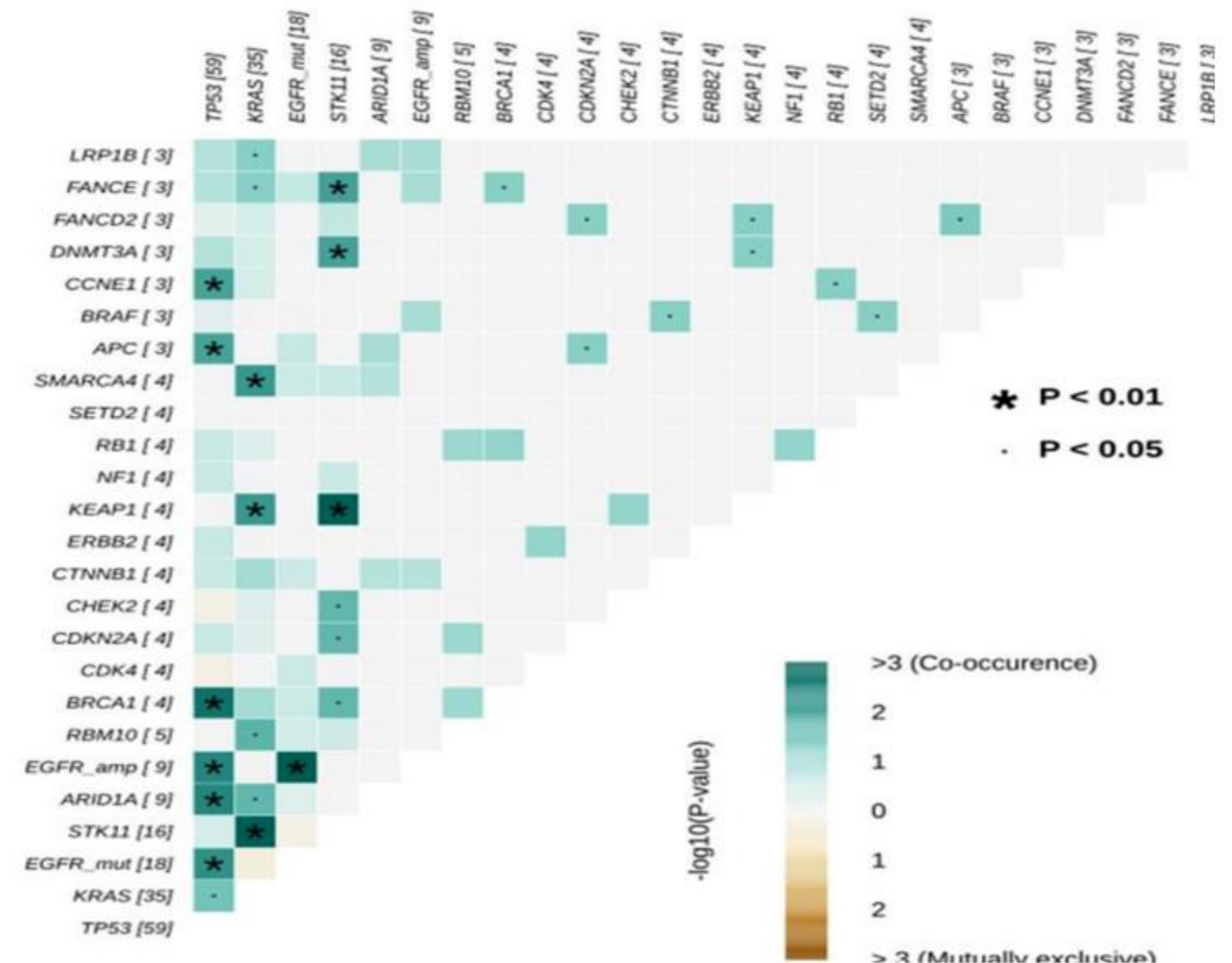
n = 137 • TP53-centered architecture



- TP53 is a central hub, with recurrent links to KRAS, ARID1A, PTEN, ATRX and RBM10.

Advanced disease (IV)

n = 134 • expanded co-mutational network



- Additional alterations involve cell cycle, DNA repair and oxidative-stress pathways; TP53–KRAS and KRAS–STK11 persist.



From a structured network to an expanded architecture

Stage progression is accompanied by additional genomic interactions and pathway involvement.

Feature	Early / locally advanced	Advanced
Network organization	Structured, TP53-centered	Expanded and more interconnected
Key associations	TP53–KRAS; KRAS–STK11; links with chromatin / DDR genes	TP53–KRAS and KRAS–STK11 persist; new interactions emerge
Pathways highlighted	DNA damage response; chromatin remodeling	Cell cycle (CCNE1); DNA repair (BRCA1/FANCE); oxidative stress (KEAP1)

Key message: genomic complexity is already present early and becomes progressively expanded in advanced disease.



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Single-gene alterations identify adverse prognostic signals

Stage-adjusted multivariable Cox models.

Overall survival

LRP1B

HR 10.21 | 95% CI 2.29–45.58
| P=0.02

STK11

HR 3.75 | 95% CI 1.33–10.59 |
P=0.025

TP53

HR 2.44 | 95% CI 1.02–5.84 |
P=0.043

Disease-free survival

STK11

HR 2.32 | 95% CI 1.18–4.55 |
P=0.023

KRAS

HR 2.16 | 95% CI 1.25–3.73 |
P=0.007

TP53

HR 1.69 | 95% CI 1.03–2.77 |
P=0.036

**STK11 and TP53 associate with both mortality
and recurrence; KRAS mainly with recurrence.**



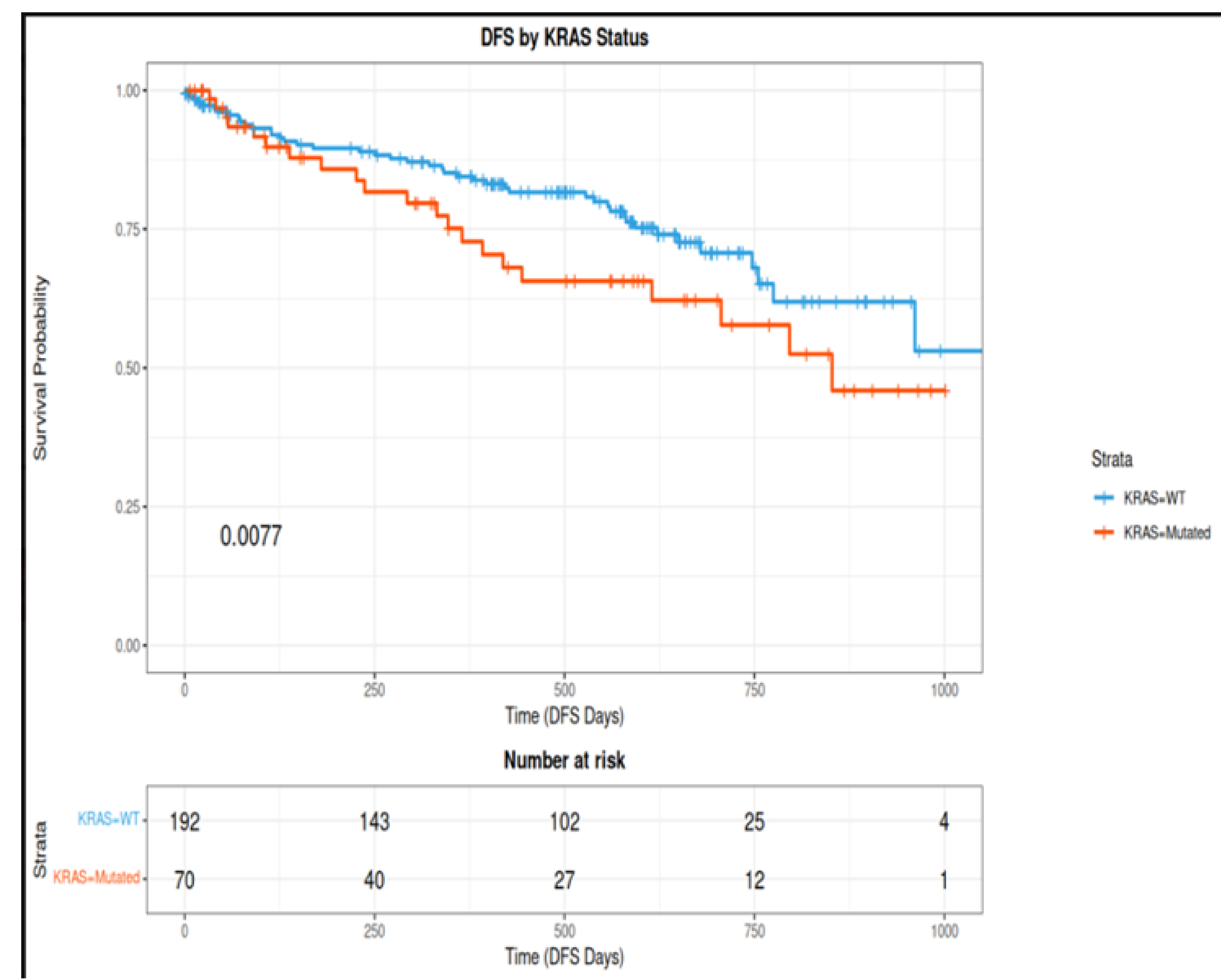
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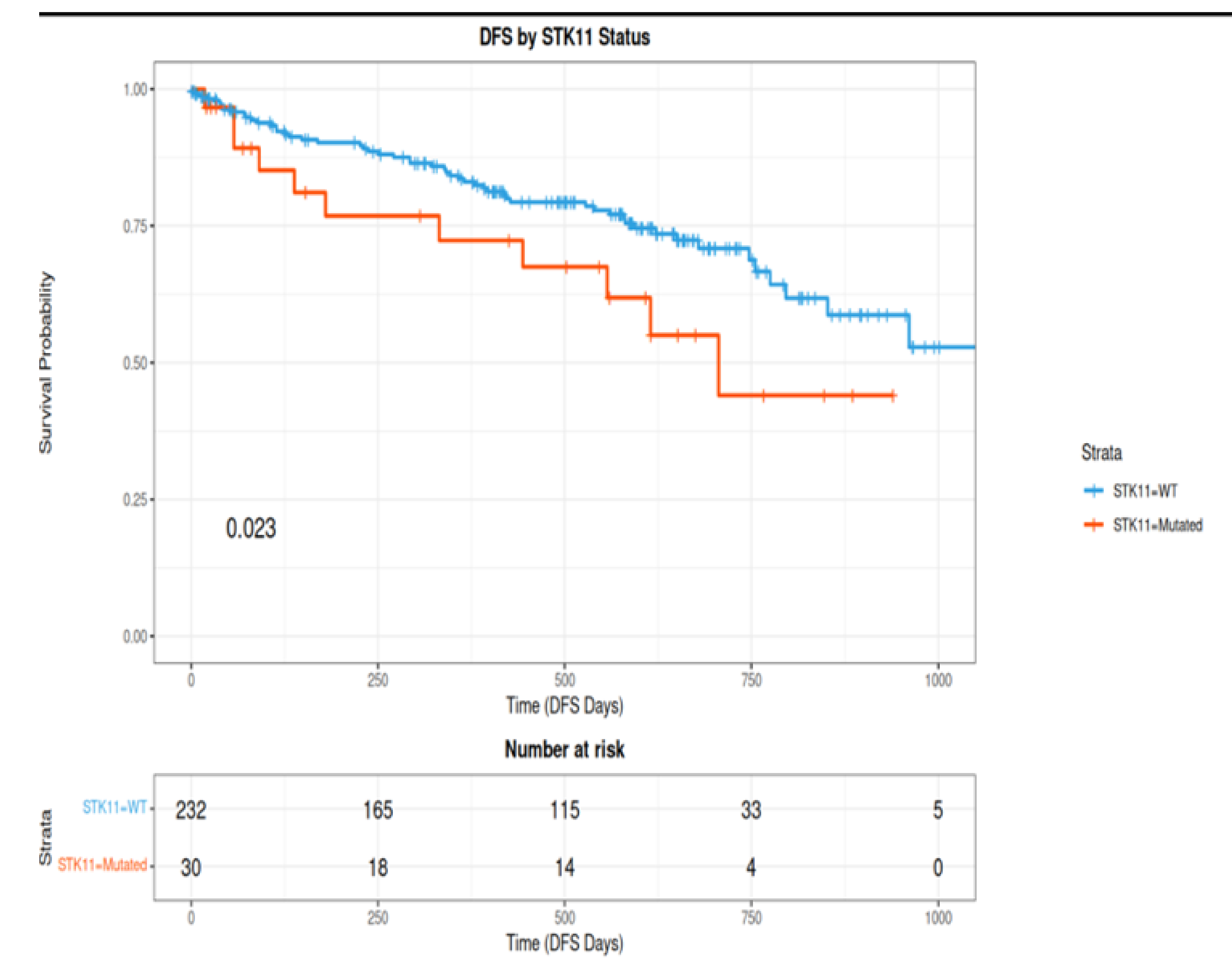


Kaplan–Meier curves

Representative DFS analyses for KRAS and STK11



KRAS mutated: P=0.0077



STK11 mutated: P=0.023



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Co-mutations sharpen prognostic stratification

Concurrent alterations often confer greater risk than single-gene status alone.

Overall survival



Disease-free survival



STK11 is the recurrent hub of adverse co-mutational profiles.



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Molecular risk is amplified by clinical context

STK11 mutation + ECOG ≥ 1

HR 10.6

95% CI 2.7–41.1 • P=0.028

**Poorest overall survival in the integrated
gene–clinical analysis**

Interpretation

Genomic and host-related factors may synergistically define aggressive disease.

Clinical relevance

Risk models may gain discriminatory power by integrating molecular status with performance status and treatment context.

Exploratory analysis — interpret in light of subgroup size and treatment heterogeneity.



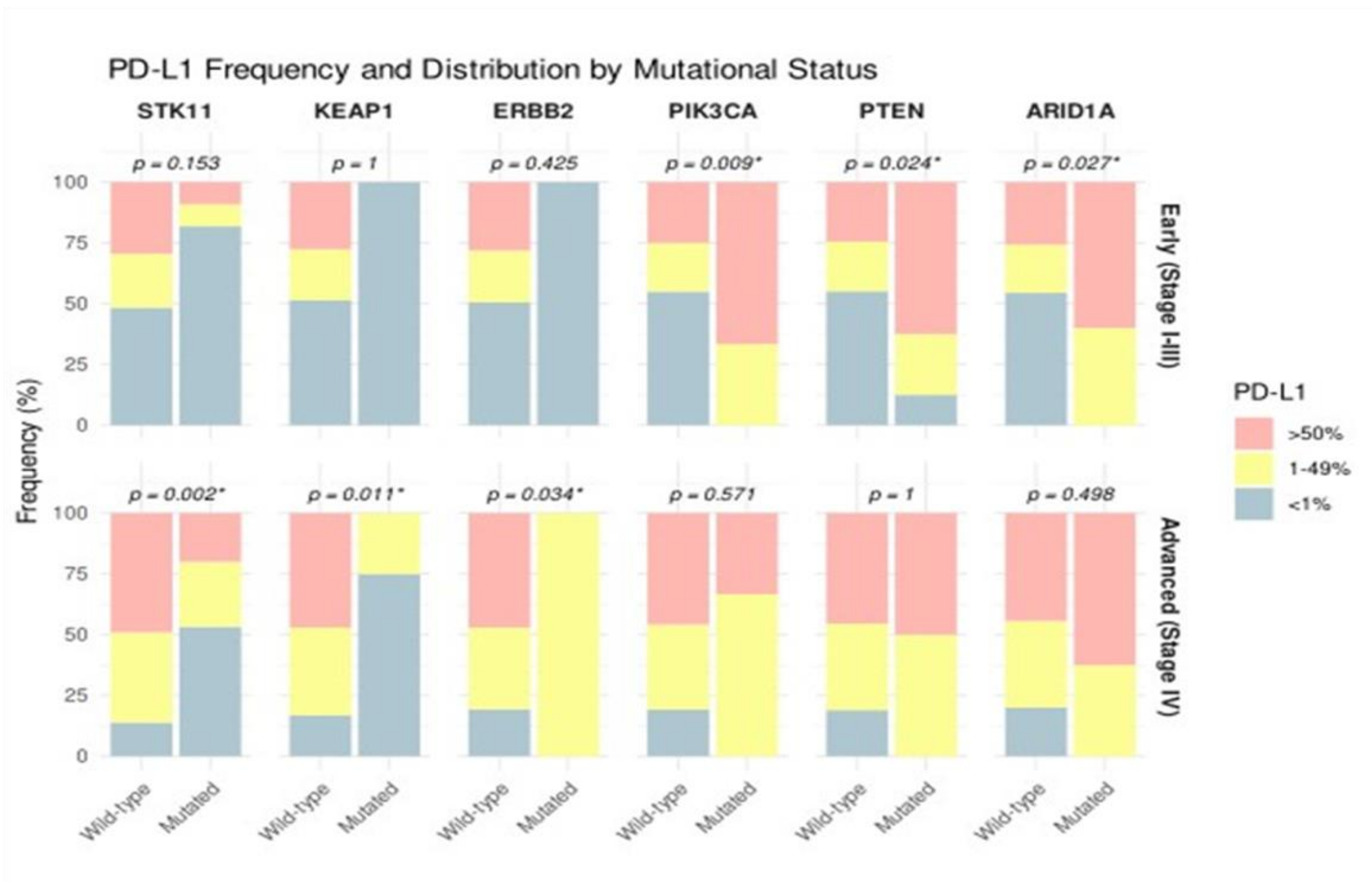
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Genomic-immune associations are stage-dependent

PD-L1 distribution differs by mutational status and disease stage.



Early stage (I-III)

PIK3CA, PTEN and ARID1A mutations → higher PD-L1 expression.

Advanced stage (IV)

STK11, KEAP1 and ERBB2 mutations → lower PD-L1 expression.

The genomic-immune relationship appears dynamic rather than fixed across progression.



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Strengths and limitations

Strengths

- Prospective, multicenter, real-world design
- Unselected cohort spanning early to advanced NSCLC
- Broad 523-gene comprehensive genomic profiling
- Simultaneous evaluation of single genes, co-mutations, PD-L1 and gene–clinical interactions

Limitations

- Heterogeneous treatment regimens across stages
- Small numbers for rare co-mutation subsets
- Wide confidence intervals for some estimates
- No independent external validation cohort
- Nominal P values without multiple-testing correction

These findings are hypothesis-generating and require prospective validation in larger independent cohorts.



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Take-home messages

1 Broad CGP matters

Clinically relevant genomic alterations are detectable across the disease continuum—not only in advanced NSCLC.

2 Context matters

STK11, TP53, KRAS and LRP1B identify adverse risk, but co-mutational patterns provide stronger prognostic discrimination.

3 Stage matters

The association between genomic alterations and PD-L1 changes with disease stage, suggesting evolution of the immune microenvironment.

From single-gene testing → toward integrated genomic risk stratification