



P1.150: Mutational Signatures and Nodal Metastasis Characteristics in Lung Adenocarcinoma with Spread Through Air Spaces

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INTRODUCTION

- Lung adenocarcinoma (LUAC)** exhibits considerable heterogeneity in clinical behavior, metastatic potential, and molecular landscape.
- Spread through air spaces (STAS)** is a unique invasive pattern and a strong predictor of poor prognosis in LUAC.
- Genetic alterations** are not only predictive of therapeutic response but also influence tumor biology, including metastatic propensity and patterns of spread.
- The interplay between **STAS and the pattern of lymph node (LN) involvement** has not been comprehensively studied.
- Study Aim:** To investigate clinicopathological and molecular signatures in STAS-positive LUAC patients and characterize the association between key driver mutations and the presence and distribution of LN metastases.

METHODS

Study Design

Single-center retrospective study

Patients

- 423 patients with surgically resected STAS+ LUAC
- Available next-generation sequencing (NGS) for driver mutations
- Detailed documentation of LN metastasis including specific LN stations involved.
- Excluded those received neoadjuvant therapy prior to surgery.

Statistical Analysis

- Mann-Whitney U test & Pearson's chi-square test for clinicopathological comparisons.
- Multivariate logistic regression to identify factors associated with LN metastasis.
- Co-occurrence network to visualize synchronous LN station involvement.

RESULTS

Driver Mutation Landscape in STAS+ LUAC

- The top three frequent oncogenic driver mutations: EGFR (53.4%), KRAS (11.1%), and ALK (7.1%).
- EGFR-mutant tumors (n=226): Predominantly female, never-smokers.
- KRAS-mutant tumors (n=47): Predominantly male, current/former smokers, higher SUVmax ($p=0.019$), higher histologic grade ($p=0.004$), lower acinar & higher solid patterns ($p=0.036$).

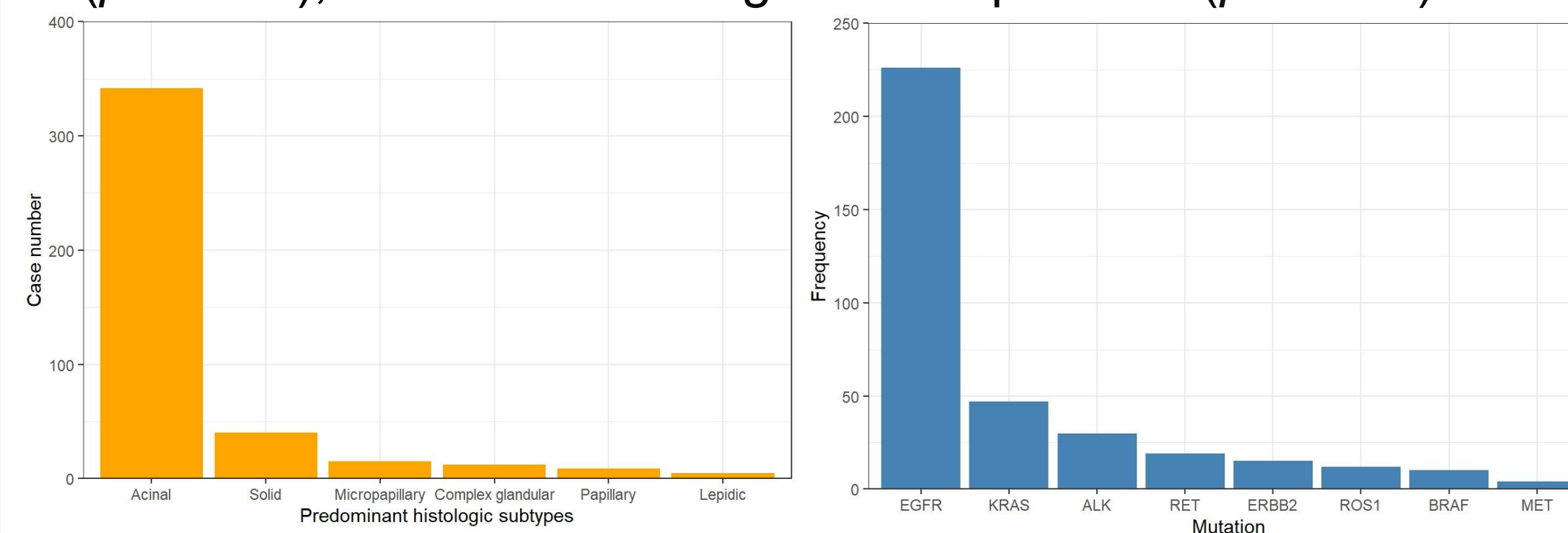


Figure 1. Distribution of predominant histologic subtypes and driver mutation in LUAC with STAS.

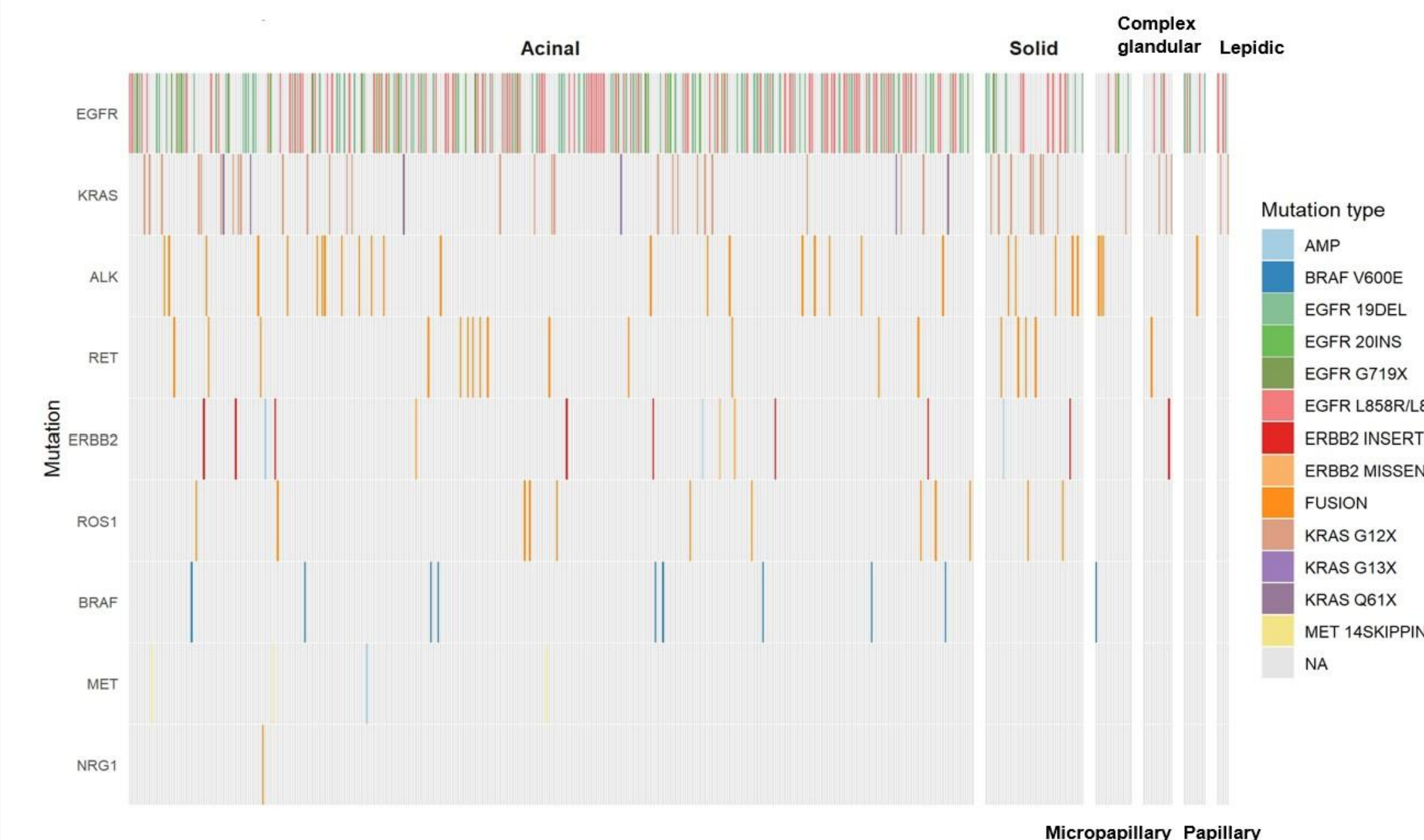
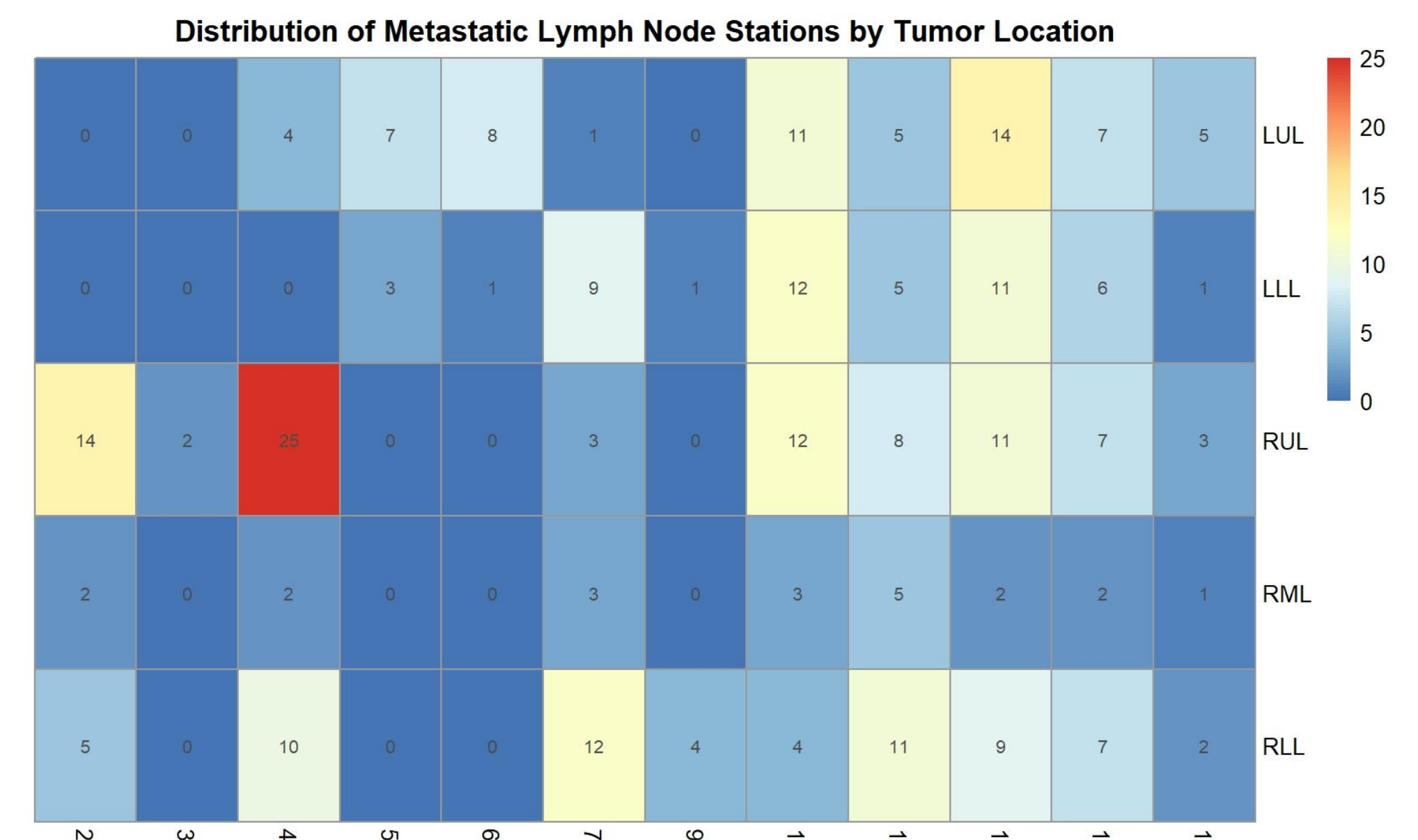


Figure 2. Mutation spectrum of STAS+ LUAC patients based on predominant histological subtypes.

Nodal Metastasis Risk Factors in STAS+ patients

Variables	OR (95% CI)	p value
CTR≤0.5	0.07 (0.00–0.38)	0.013
Histologic grade 3 (reference to grade 2)	1.13 (0.48–2.61)	0.774
pT1c stage (reference to pT1a-1b)	2.07 (1.01–4.26)	0.046
pT2a or higher stage (reference to pT1a-1b)	1.64 (0.68–3.94)	0.265
Percentage of lepidic component	0.99 (0.93–1.04)	0.631
Percentage of acinar component	1.01 (0.98–1.03)	0.633
Percentage of papillary component	0.97 (0.92–1.01)	0.123
Percentage of solid component	0.99 (0.97–1.02)	0.527
Percentage of micropapillary component	1.02 (0.98–1.05)	0.323
Presence of LVI	8.84 (3.84–21.90)	<0.001
VPI (PL1) (reference to PL0)	1.87 (0.74–4.70)	0.183
VPI (PL2) (reference to PL0)	1.33 (0.39–4.40)	0.640
VPI (PL3) (reference to PL0)	0.99 (0.04–14.03)	0.993
PD-L1 TPS score	1.01 (1.00–1.03)	0.039
Ki67 level	1.02 (1.00–1.03)	0.020

CTR, consolidation-tumor ratio; LVI, lymphovascular invasion; VPI, visceral pleural invasion.



CONCLUSION

- Identified **key driver mutation signatures** and **associated factors of nodal metastasis** in STAS+ LUAC.
- Station-specific metastasis** by primary tumor location highlighted the importance of anatomically tailored LN dissection strategies.
- Integrating **molecular profiling with pathological mapping** enhances risk stratification in STAS+ LUAC.

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