

P3.236: Real-World Outcomes of Advanced ALK-positive Lung Cancer: Prognostic Role of Molecular Subvariants and Systemic Inflammation

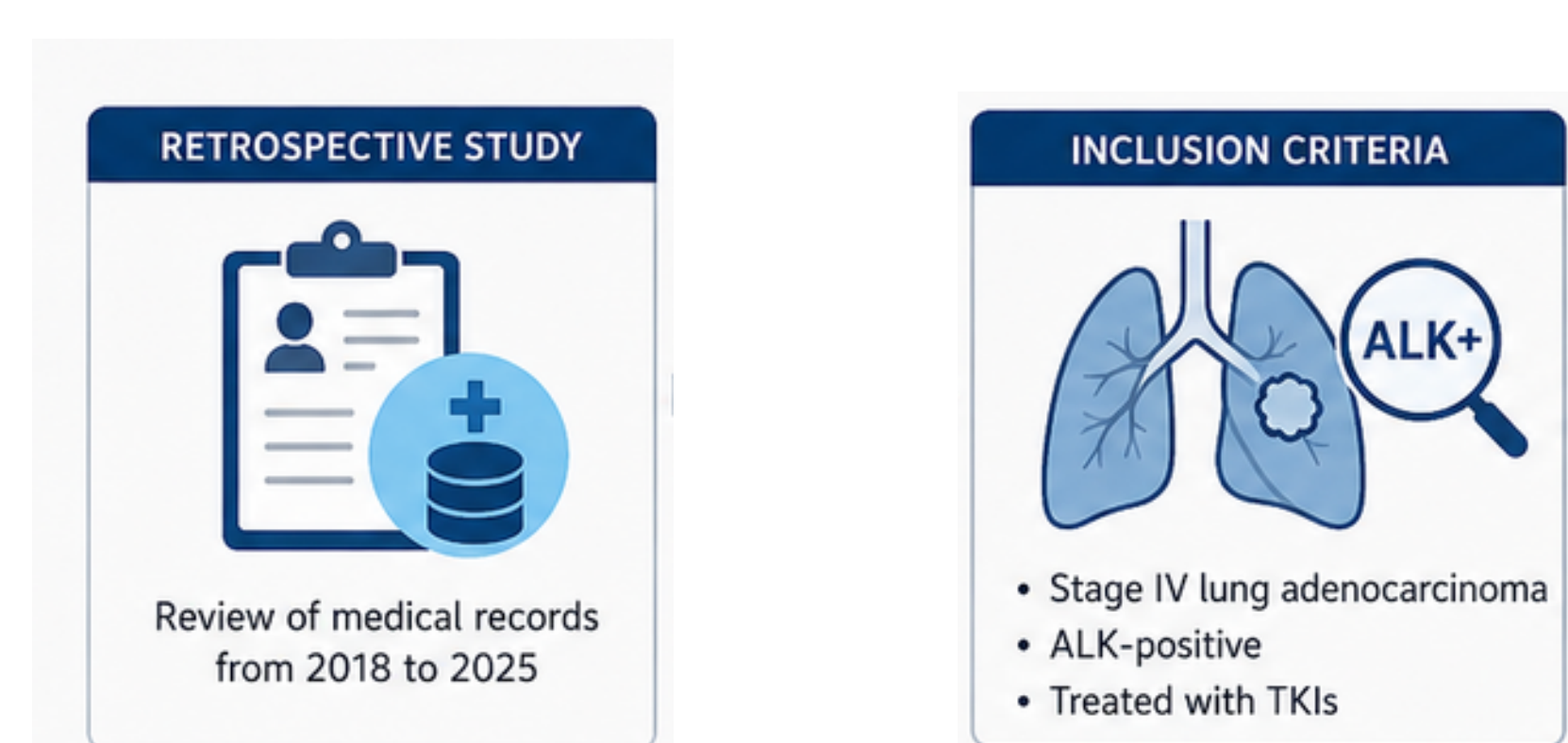
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INTRODUCTION

- ALK-rearranged non-small cell lung cancer (NSCLC) demonstrate sensitivity to targeted therapies.
- However, clinical outcomes remain heterogeneous, potentially influenced by specific ALK subvariants and host-related factors such as systemic inflammation.

METHODS



Design:

- A retrospective study was conducted including patients diagnosed with stage IV ALK-positive lung adenocarcinoma treated with tyrosine kinase inhibitors (TKIs) at Hospital Universitario San Cecilio between 2018 and 2025.
- The cohort was characterized in terms of demographic and molecular features, and multiple statistical analyses were performed.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- ALK molecular subvariants may identify patients with distinct clinical outcomes, with non-classical/unclassified variants showing poorer survival in our real-world cohort.
- Integrating molecular and readily available clinical biomarkers (NLR) may improve risk stratification beyond ALK positivity alone.

Future Direction for Research

- Larger datasets are required to determine whether molecular subvariants can also predict differential benefit from specific ALK TKIs.

REFERENCES & ACKNOWLEDGEMENTS

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RESULTS

- 813 patients, we assembled a cohort of 36 patients ALK+. The cohort included 17 (47,2%) male and 19 **(52,7%) female patients. Median age of 68 years** (32–87 years). **About 91.6% of patients presented advanced stage.**
- The most frequent genetic alteration was the **EML4(13)–ALK(20) fusion (variant 1, 19.15%) (Fig1). The median overall survival (OS) for the entire cohort was not reached for variants 1 and 2. For variant 3, median OS was 26.6 months (0–44.3),** whereas **unclassified variants-non classical had a poorer prognosis with a median OS of 10.2 months (1.1–24.2) (p = 0.03).**
- The median progression-free survival (PFS) for the overall population was 14.2 months (2.0–22.6). Variant 1: 24.3 month, Variant 2: 40.3 months, Variant 3: 21.5 months, unclassified variants-non classical: 2.1 months
- **Brain metastases were not associated with prognosis in this cohort.**
- Kaplan–Meier analysis did not show statistically significant differences between the second-generation and third-generation inhibitors in either OS (p = 0.75) or PFS (p = 0.51).
- In multivariate Cox analysis, **elevated NLR** remained a significant adverse prognostic factor (p = 0.0014), while **variant 3 and unclassified variants showed a trend toward worse outcomes. Variant 2 appeared to be associated with the most favorable prognosis.** Although patients treated with third-generation inhibitors appeared to have fewer events and they were also younger, suggesting potential confounding factors.

