

# P2.227: Clinical Fragility and Prognostic Stratification in *Stk11*/LKB1 Impaired NSCLC: Insights From a Real-World Cohort

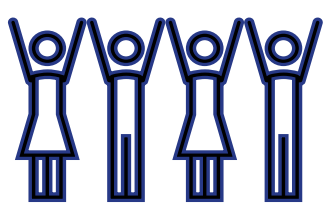
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## INTRODUCTION

*Stk11*/LKB1 alterations occur in 15–18% of advanced NSCLC and define an aggressive subset, characterized by suboptimal benefit from immune checkpoint inhibitors (IO).

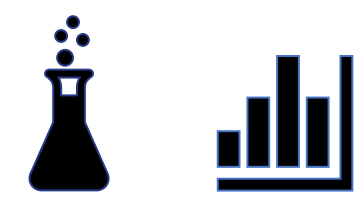
We conducted a clinical, genomic, and exploratory biomarker analysis in a large real-world cohort of advanced *STK11*/LKB1-impaired NSCLC.

## METHODS



**196 patients** *Stk11*/LKB1, stage IV NSCLC from 2019 to 2025, monocentric.

*Stk11*/LKB1 impaired phenotype: **loss of protein** expression (IHC) or presence of any kind of *Stk11* **mutation** (NGS).



Lipidomic: Cobas Roche automated clinical chemistry analyzer and GC system (Shimadzu), in plasma.

Metabolomic: MxP Quant 500 Biocrates kit on the 5500 TRIPLEQUAD mass spectrometer (AB Sciex), in FFPE tumor tissue.

OS: from diagnosis of metastatic disease to death; PFS: from metastatic treatment start to disease progression/ death.

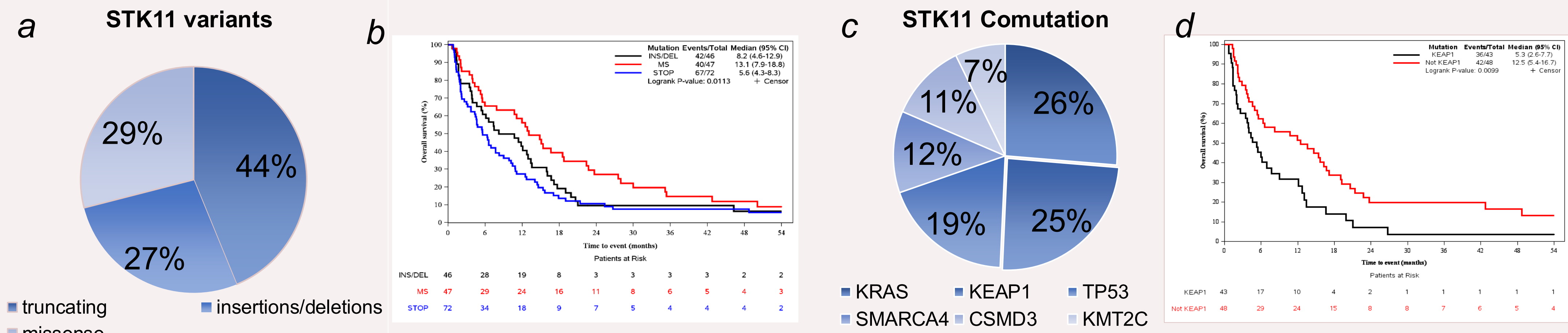
## ACKNOWLEDGEMENTS

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## RESULTS

**Median OS was 7.7 months** (95%CI 6.4–11.1), with no difference due to treatment received as first line or to the kind of *Stk11*/LKB1 alteration (*Fig1*).

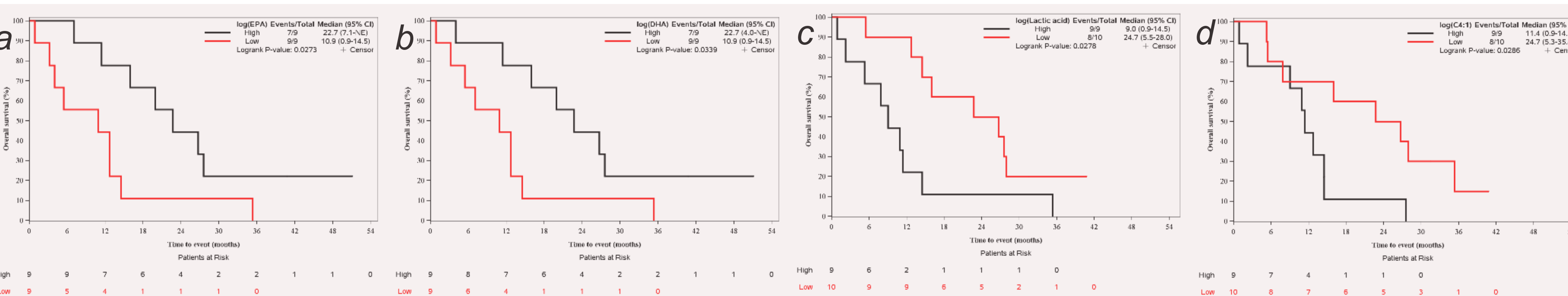
**OS was shorter** in patients with **truncating mutations** (5.6 months,  $p=0.01$ ) (*Fig2b*), in **Keap1** (5.3 months,  $p<0.01$ ) (*Fig2d*), and **SmarcA4** (4.0 months,  $p=0.05$ ).



**Figure 2** a. *STK11* types of variants, b. Kaplan Meyer curves according to variants, c. *Stk11* most frequent co-altered genes, d. Kaplan Meyer curves according to *Keap1* mutation.

OS was significantly influenced by ECOG PS ( $p<0.01$ ) and adenocarcinoma histology ( $p=0.03$ ), as expected (data not shown).

Patients with **lower eicosapentaenoic acid** (EPA, C20:5) and **docosahexaenoic acid** (DHA, C22:6) on plasma showed **shorter OS** (10.9 vs 22.7 months,  $p=0.03$ ), for both lipids (*Fig3 a,b*).



**Figure 3.** Kaplan Meyer curves according to EPA(a), DHA(b), lactate(c), butenylcarnitine(d) levels.

Patients with **higher levels of lactate** and **butenylcarnitine** (C4:1) experienced **shorter OS** (9.0, 11.4 vs 24.7, 24.7 months, respectively,  $p=0.03$ ) (*Fig3 c,d*).