1477P - STK11 mutations predict poor prognosis for advanced NSCLC treated with first-line immunotherapy or chemo-immunotherapy according to KRAS, TP53, KEAP1, and SMARCA4 status

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INTRODUCTION

The upfront treatment of non-small-cell lung cancer (NSCLC) relies on immunotherapy single-agent (IO) or in combination with chemotherapy (CT-IO)24. Genomic aberrations such as KRAS, TP53, KEAP1, SMARCA4, or STK11 may impact the survival of patients25,26. However, some clinical trials demonstrated that the mutational status of KRAS, TP53, KEAP1, SMARCA4, and STK11 genes could be predictive for different outcomes when treated with the same line of therapy27,28. The prognostic role of STK11 mutations (mut) under upfront IO treatment in NSCLC pts is still debated.

RESULTS

In the internal cohort, most pts were male (59.7%), former smokers (61.1%), and 67.7% with ECOG 0-1 (84%), and received first-line CT-IO (58.6%). 44.8% had a mutation in KRAS, 21.4% in KEAP1, 50.3% in TP53, 13.1% in SMARCA4, and 14.4% in the STK11 gene. 14/21 pts STK11 and KRAS mut co-occur (p=0.053). The median overall survival (OS) was 13.2 months (mo.) (95% CI, 8.6-19.6), while the median progression-free survival (PFS) was 6.5 mo. (95% CI, 4.8-8.9). The mOS was 8 mo. (95% CI, 5-16.7) for STK11 mut pts and 17.3 mo. for STK11 WT pts (95% CI, 8.9-24.4) (p=0.038). TP53 (8.3 vs 17.3), KRAS (9.2 vs 15.9), and KEAP1 (8.9 vs. 15.9) mut patients evidenced a trend for dismal mOS. STK11 mut did not impact the mPFS in our cohort.

MATERIALS AND METHODS

Observational study of patients (pts) treated with first-line IO or CT-IO for advanced nonsquamous (nsq) NSCLC at our institution (Internal cohort).

In addition to baseline NGS analysis, archival specimens were re-tested with a NGS panel developed in the Molecular Pathology Laboratory of IRCCS Ospedaliero-Universitaria di Bologna.

In particular, the entire coding region of the following genes was analyzed: KEAP1, SMARCA4, STK11, and TP53. The pathogenicity of each mutation was assessed using the Varsome tool.

External validation through the public OAK/POPLAR dataset of liquid biopsies2, including nsq NSCLC pts treated with second-line atezolizumab or CT (Validation Cohort).

The primary objective was to assess the clinical outcomes of STK11 mutated pts according to KRAS, TP53, KEAP1, and SMARCA4 status.

REFERENCES

1. De Giglio A et al., DIC, 2022
2. Gandara DR et al., Nat Med, 2018

CONCLUSIONS

STK11 mut hampered the mOS of nsq NSCLC pts treated with first-line IO or CT-IO. STK11 mut was an independent prognostic factor for OS in both internal and validation cohorts regardless of the type of treatment (IO, CT-IO, CT), co-mutations, and clinical factors.

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DISCLOSURE

The presenting author has no conflicts of interest.

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