

KEAP1/STK1/KRAS co-alterations promote central nervous system (CNS) metastasis in lung adenocarcinoma and are associated with primary therapy resistance

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Summary



STK11/KEAP1/KRAS co-alterations in LUAD are associated with a high incidence of CNS metastases and primary resistance to treatment, underscoring the need for novel therapeutic approaches.

Background

- STK11/KEAP1/KRAS co-alterations are associated with an immunological cold and biologically aggressive lung adenocarcinoma (LUAD) subtype.¹
- There is limited data on the impact of these hard- to-treat alterations on the incidence of central nervous system (CNS) metastases.²

Methods

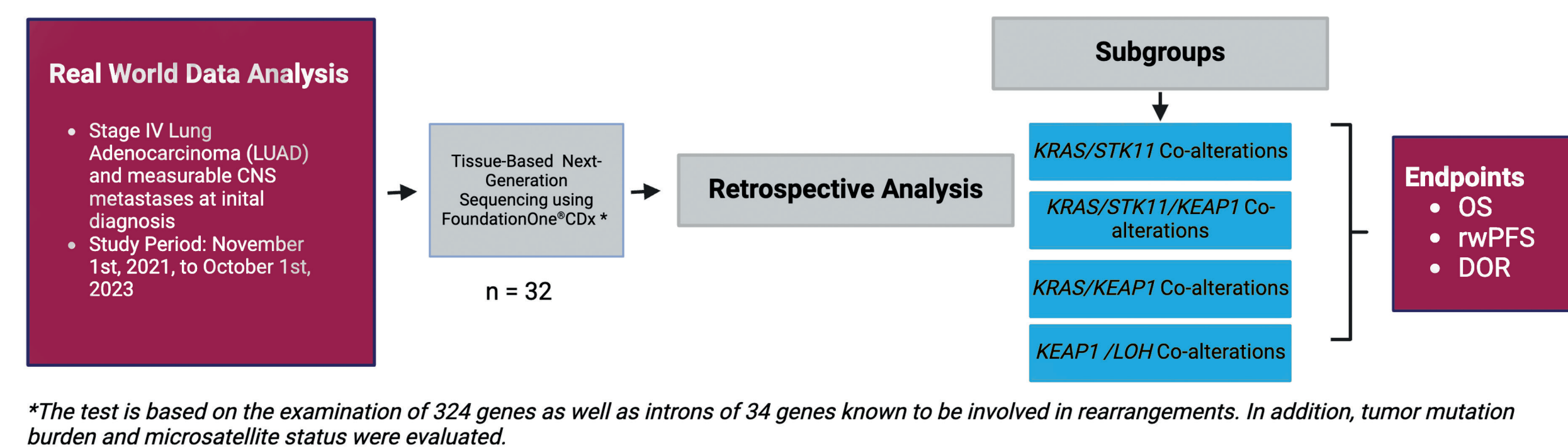


Figure 1: Study Design.

Results

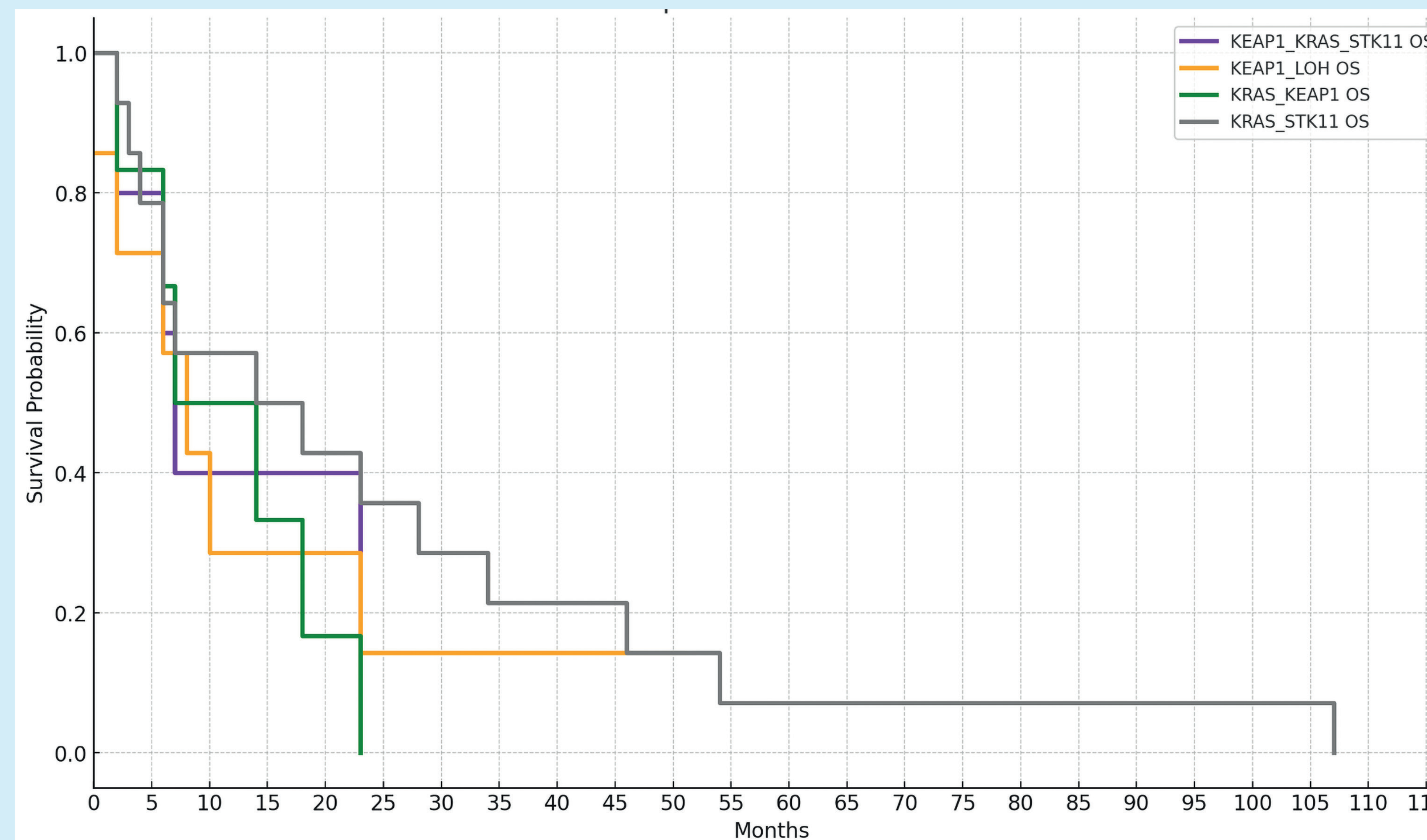


Figure 2: Overall Survival of Analyzed Subgroups

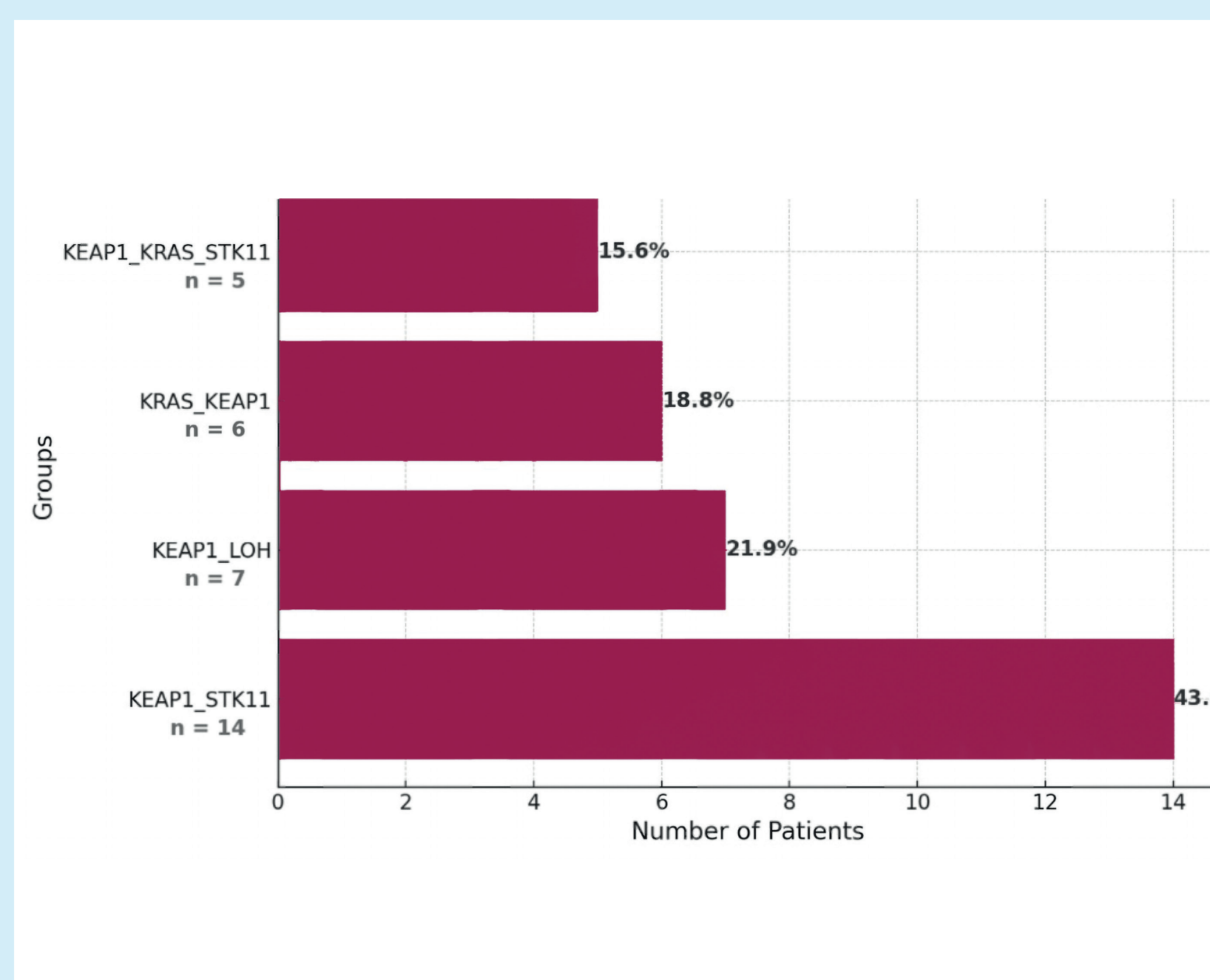


Figure 3: Distribution of Patients across the Analyzed Subgroup

Age	67 (±9.7)
Sex	
Male	19 (59.4%)
Female	13 (40.6%)
PD-L1 status	
50-100%	2 (6.3%)
5-50%	3 (9.4%)
1-5%	10 (31.2%)
<1%	16 (50%)
Unknown	1 (3.1%)
Systemic Therapies	
Carboplatin/Pemetrexed/Pembrolizumab	27 (84.4%)
Pembrolizumab	3 (9.4%)
Carboplatin/Pemetrexed	2 (6.2%)
Stereotactic Radiation for Brain Metastases at initial diagnosis	8 (25%)
Neurosurgical Intervention at initial diagnosis	6 (18.8%)

Table 1: Demographics and Baseline Characteristics

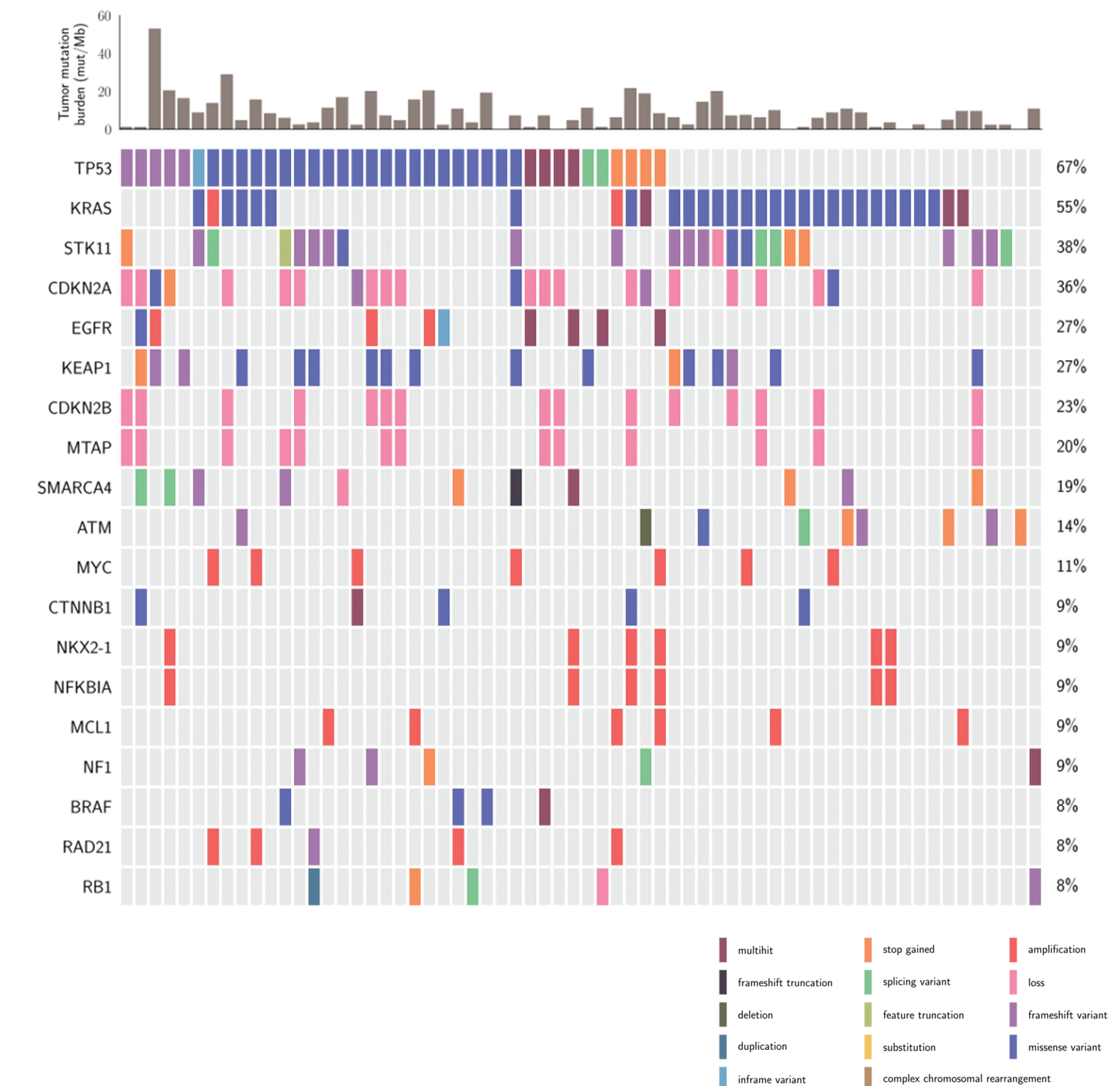


Figure 4: Oncoplot of Analyzed Patient Cohorts with STK11/KEAP1/KRAS Mutations According to Tumor Mutational Burden (TMB)

Conclusion



- Our findings based on real-world data indicate that STK11/KEAP1/KRAS co-mutations are hard-to-treat alterations that coincide with primary CNS metastases, especially in the STK11/KEAP1/KRAS-mutated or KEAP1 LOH-mutated subgroups.
- The short rwPFS associated with primary therapy resistance underline the unmet need for new therapeutic strategies.

1. Ricciuti B., et al. J thorac Oncol. 2022 Mar;17 (3):399-410
2. Eichholz, J. et al. International Journal of Radiation Oncology, Biology, Physics, Volume 117, Issue 2, e101 - e102.