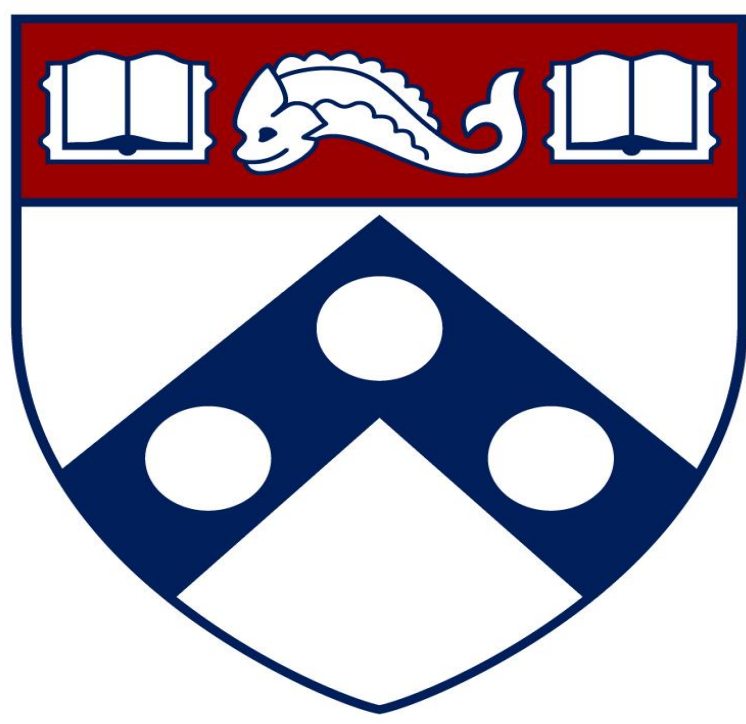




P1.283: Clinical Outcomes and Prognostic Factors in Stage IV SMARCA4-Mutant NSCLC

Brian Andres Robusto, Lova Sun, Aditi Singh, Willdragon Wang, Daniel Huth, Xiaoke Wang, Christiana Davis, Corey K. Langer, Roger B. Cohen, Charu Aggarwal, Melina Marmarelis

Hospital of the University of Pennsylvania, Philadelphia, PA

Correspondence: Melina.Marmarelis@pennmedicine.upenn.edu



IASLC 2026 World
Conference on Lung Cancer

SEPTEMBER 12 – 15, 2026
SEOUL, REPUBLIC OF KOREA

INTRODUCTION

- SMARCA4-mutant (SM) NSCLC is a rare molecular subtype associated with aggressive disease biology and poor clinical outcomes.
- Contemporary data describing outcomes in patients treated with immune checkpoint inhibitor–based therapy remain limited.
- The prognostic impact of common genomic co-mutations (e.g., TP53, STK11, KRAS) has not been well characterized.
- We evaluated clinical outcomes and prognostic factors in a contemporary cohort of patients with stage IV SMARCA4-mutant NSCLC.

METHODS

STUDY DESIGN

Single-center retrospective cohort study conducted at the University of Pennsylvania. Clinical data were abstracted from the electronic medical record. Survival analyses were performed using Kaplan–Meier methods with log-rank testing and Cox proportional hazards regression. Statistical significance was defined as two-sided $P < 0.05$.



PATIENT IDENTIFICATION

80 patients

Stage IV
SMARCA4-mutant NSCLC
Aug 2016–Dec 2025



PRE-TREATMENT MORTALITY

15

Died before systemic therapy



TREATED COHORT

65

Received first-line systemic therapy



OUTCOMES & STATISTICS

- Overall Survival
- Progression-Free Survival
- Kaplan–Meier
- Log-rank test
- Cox regression

CLINICAL VARIABLES COLLECTED

- Demographics
- Smoking history
- Histology
- ECOG performance status
- PD-L1 expression
- Brain metastases
- TP53, STK11 and KRAS co-mutations
- First-line systemic therapy

DISCUSSION AND CONCLUSION

- 19% of patients died before systemic therapy with a median OS of 1.1 months**, underscoring the aggressive natural history of stage IV SM-NSCLC.
- 53% of the patients who died before receiving systemic therapy were Black**, despite Black patients making up a much smaller proportion of the overall cohort.
- Median OS was 12.2 months and median PFS was 7.9 months** among treated patients receiving contemporary systemic therapy.
- Median OS** by treatment group was **10.7 months** for chemoimmunotherapy, **18.3 months** for ICI monotherapy, and **3.8 months** for chemotherapy alone.
- TP53 co-mutations were associated with improved overall survival**, while **STK11 co-mutations** and baseline brain metastases were associated with poorer outcomes.
- Poor ECOG performance status was associated with inferior survival**, highlighting functional status as an important prognostic factor in this population.
- Early mortality remains a major challenge** in stage IV SMARCA4-mutant NSCLC.
- Future multi-institutional studies should evaluate **clinical, molecular, and health equity–related** factors that contribute to early mortality in SMARCA4-mutant NSCLC.
- Co-mutation status may improve prognostic risk stratification** and should be evaluated in future prospective studies.

REFERENCES & ACKNOWLEDGEMENTS

- Ricciuti B, Alessi JVM, et al.** SMARCA4 and Other SWI/SNF Family Genomic Alterations in NSCLC: Clinicopathologic Characteristics and Outcomes to Immune Checkpoint Inhibition. J Thorac Oncol. 2021.
- Zhou H, Shen J, Liu J, Fang W, Zhang L.** Efficacy of Immune Checkpoint Inhibitors in SMARCA4-Mutant NSCLC. J Thorac Oncol. 2020.
- Zhao W, Guan M, Zhang H, et al.** Clinical outcomes and tumor immune microenvironment in SMARCA4-deficient NSCLC: A real-world retrospective study. Lung Cancer. 2026.



Please scan this QR
code for more
information.

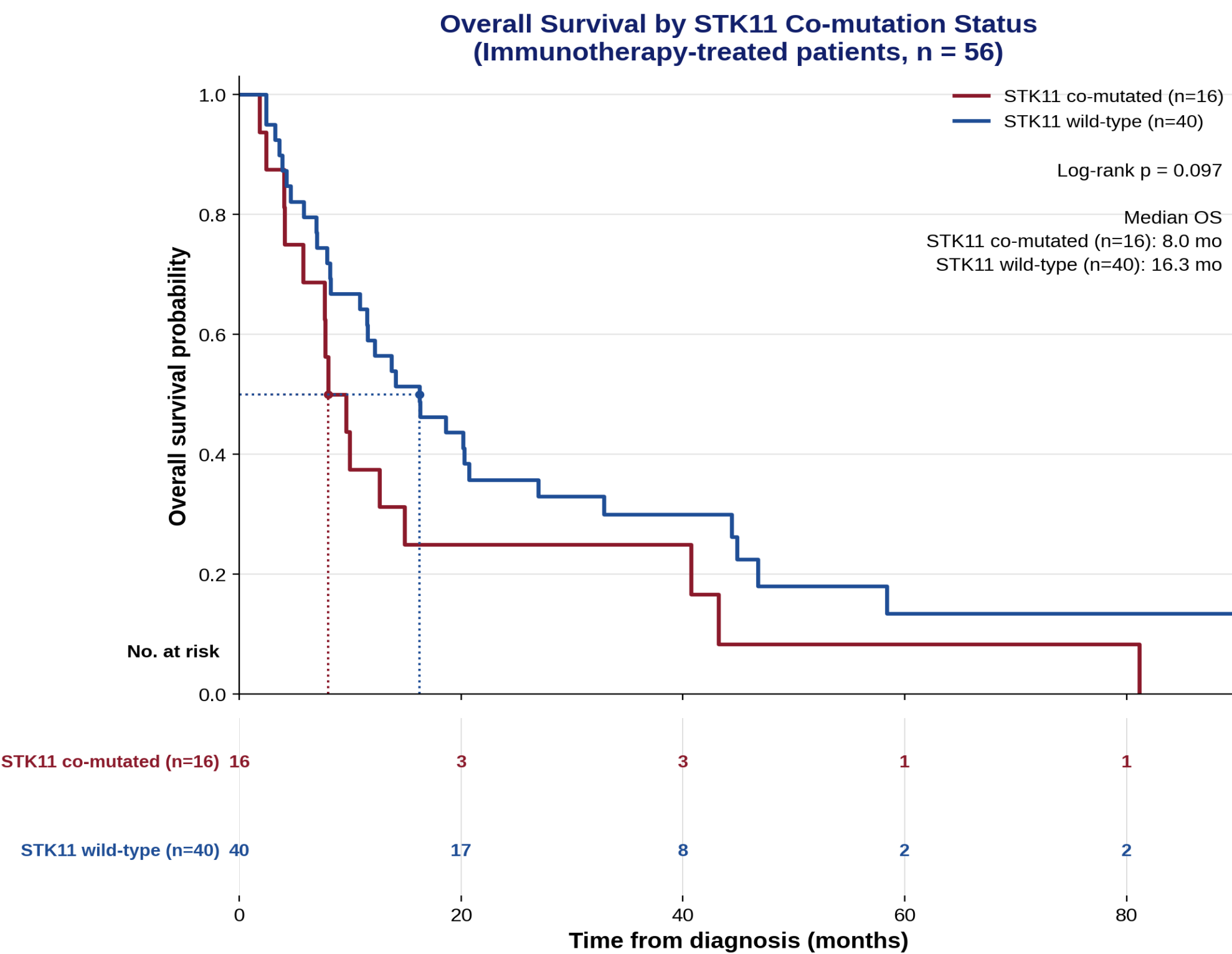
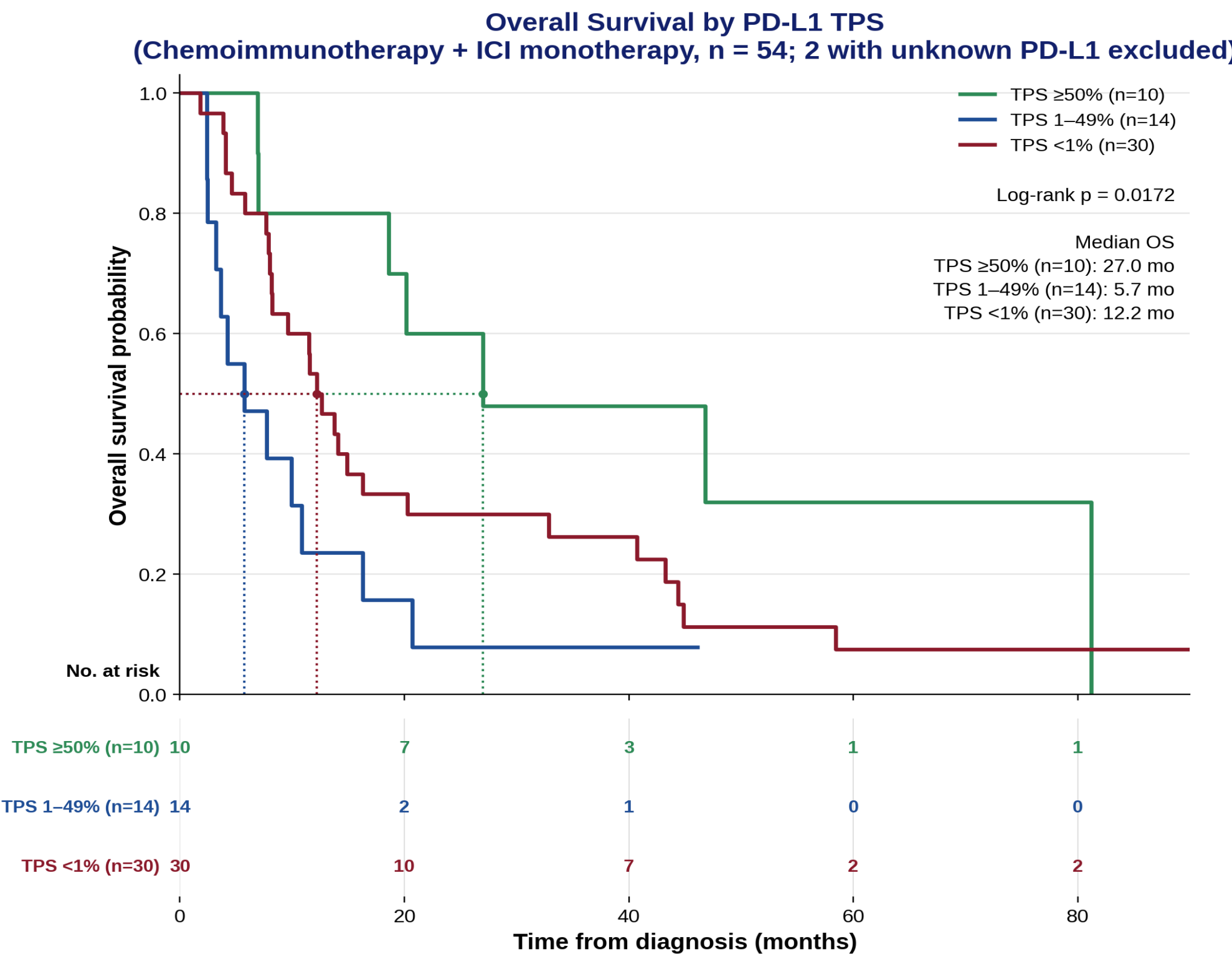
We thank the patients and families whose clinical data made this study possible. We acknowledge the faculty and staff of the Hospital of the University of Pennsylvania and Abramson Cancer Center for their mentorship and support. We also thank the Division of Precision & Computational Diagnostics for their data collection.

This study was conducted with approval from the University of Pennsylvania Institutional Review Board.

Artificial Intelligence Disclosure: Claude (Anthropic) assisted in the creation of Kaplan–Meier survival curves and in editing presentation content. All data analyses and final scientific interpretations were verified by the authors.

RESULTS

Characteristic	Treated patients (n = 65)
Age at diagnosis, median (range), y	67 (46–87)
Sex, n (%)	
Male	36 (55.4%)
Female	29 (44.6%)
Race, n (%)	
White	47 (72.3%)
Black	14 (21.5%)
Other/Unknown	4 (6.2%)
Ever smoker, n (%)	63 (96.9%)
Histology, n (%)	
Adenocarcinoma	26 (40.0%)
Poorly differentiated NSCLC	31 (47.7%)
Squamous cell carcinoma	2 (3.1%)
Other	6 (9.2%)
ECOG PS at treatment start, n (%)	
0	21 (32.3%)
1	28 (43.1%)
≥2	16 (24.6%)
Brain metastases at baseline, n (%)	20 (30.8%)
STK11 co-mutation, n (%)	18 (27.7%)
TP53 co-mutation, n (%)	43 (66.2%)
First-line treatment, n (%)	
Chemoimmunotherapy	45 (69.2%)
ICI monotherapy	11 (16.9%)
Chemotherapy alone	9 (13.8%)



Variable	Univariable HR (95% CI)	p	Multivariable HR (95% CI)	p
Age (per year)	1.03 (1.00–1.07)	0.022	1.03 (0.99–1.07)	0.123
ECOG PS (per unit)	2.36 (1.68–3.30)	<0.001	3.10 (2.01–4.79)	<0.001
Brain metastases (yes vs no)	1.75 (0.95–3.21)	0.072	2.05 (1.03–4.10)	0.041
STK11 co-mutation (yes vs no)	1.48 (0.83–2.63)	0.188	1.08 (0.58–2.03)	0.806
TP53 co-mutation (yes vs no)	0.45 (0.25–0.81)	0.008	0.38 (0.19–0.78)	0.008
Male sex (vs female)	0.85 (0.50–1.44)	0.539	1.04 (0.55–1.97)	0.900
Black race (vs non-Black)	0.70 (0.36–1.36)	0.287	0.54 (0.24–1.24)	0.148
Chemoimmunotherapy (vs chemo alone)	0.93 (0.52–1.65)	0.807	2.32 (0.88–6.08)	0.087
ICI monotherapy (vs chemo alone)	0.66 (0.31–1.40)	0.281	0.96 (0.35–2.62)	0.929

