



P2.077-248: Clinical-Genomic Characteristics of MTAP Loss in a Nationwide Veterans Affairs Lung Cancer Cohort

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INTRODUCTION

- Loss of methylthioadenosine phosphorylase (*MTAP*), often co-occurring with *CDKN2A/CDKN2B* alterations, is a recurrent genomic event in lung cancer with emerging therapeutic relevance.
- The veteran population differs in demographics, comorbidities, and tumor characteristics from the non-veteran population.
- Defining the clinical-genomic landscape in this national veteran cohort is essential to inform clinical trial planning and population selection.

METHODS

- Veterans with non-small cell lung cancer (NSCLC) who underwent next-generation sequencing through the Department of Veterans Affairs (VA) National Precision Oncology Program (NPOP) between February 2, 2019, and October 30, 2025, were retrospectively identified by ICD-O-3 histology and topology codes.
- Vendor panels included in this study were the Tempus xT and FoundationOne CDx tissue tests.
- Demographic information was obtained from the VA's Corporate Data Warehouse (CDW).
- Tumor-specific data elements not available in the NPOP database were obtained from CDW oncology raw tables, confirmed by ICD-O-3 code, and linked by a unique patient identifier. *MTAP* status was defined as “loss” if the alteration was categorized by the vendor as “LOF”, “loss”, or “deletion. *MTAP* status was defined as “intact” if no alterations were reported on the test, or if the alteration was categorized by the vendor as anything other than the “loss” category (could include rearrangements and SNPs).

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- These findings provide real-world estimates of *MTAP* loss in a representative veteran population and highlight a substantial subset of patients who may be eligible for emerging *MTAP*-targeted therapeutic strategies.
- MTAP* loss may define a biologically distinct subset of lung cancer, but it does not serve as an independent prognostic marker for survival in US Veterans.

Future Direction for Research

- Further studies will include determination of whether *MTAP* loss is associated with efficacy of various treatments for NSCLC.

REFERENCES & ACKNOWLEDGEMENTS

- Ross JS, Thummalapalli R, Febres-Aldana CA, et al. Clinical Significance of *MTAP* Deletions and Their Overlap With Concurrent Oncogenic Driver Alterations Including *EGFR* in NSCLC. *J Thorac Oncol.* 2026;21(3):103520. doi:10.1016/j.jtho.2025.11.010
- Ashok Kumar P, Graziano SL, Danziger N, et al. Genomic landscape of non-small-cell lung cancer with methylthioadenosine phosphorylase (*MTAP*) deficiency. *Cancer Med.* 2023;12(2):1157-1166. doi:10.1002/cam4.4971
- Ikushima H, Watanabe K, Shinozaki-Ushiku A, Oda K, Kage H. Clinicogenomic Landscape of *MTAP*-Deleted Thoracic Malignancies Across US and Japanese Nationwide Cohorts: Impact of Concurrent *CDKN2A* Alterations and Driver Mutations. *JCO Precis Oncol.* 2026;10(5):e2600100. doi:10.1200/PO-26-00100
- Ikushima H, Watanabe K, Shinozaki-Ushiku A, Oda K, Kage H. Clinicogenomic Landscape of *MTAP*-Deleted Thoracic Malignancies Across US and Japanese Nationwide Cohorts: Impact of Concurrent *CDKN2A* Alterations and Driver Mutations. *JCO Precis Oncol.* 2026;10(5):e2600100. doi:10.1200/PO-26-00100
- Huang J, Aldea M, Miller KW, Rotow JK, Mazzola E, Nishino M, Sholl LM, Jänne PA, Barbie DA, Shaw AT, Kehl KL, Luo J. Presenting features and outcomes to standard systemic therapies in patients with *MTAP*-deleted advanced non-small cell lung cancer. *Clin Cancer Res.* 2026 Jul 6;10.1158/1078-0432.CCR-26-0188. doi: 10.1158/1078-0432.CCR-26-0188. Epub ahead of print. PMID: 42405849; PMCID: PMC13422915.

Artificial Intelligence (AI) Use Disclaimer

Generative AI was used only for grammar and sentence-structure editing; all content and interpretations are the authors' own.

RESULTS

- 5734 NSCLC cases with our inclusion criteria underwent NGS testing through NPOP
- MTAP* loss was identified in 798 (13.4%) patients.
- Based on multivariate Cox regression modeling, factors independently associated with overall survival (OS) included: Advanced age (HR 1.02; 95% CI 1.01-1.03, p<0.001), presence of actionable mutations (HR 0.80; CI 0.70-0.92, p=0.002), Charlson Comorbidity Index≥ 3 (HR 1.27; CI 1.08-1.51, p=0.005), and high TMB (HR 0.79; CI 0.71-0.88, p<0.001).
- MTAP* loss was not independently associated with OS (HR 1.00; 95% CI 0.86–1.16; p=0.995).

	Overall n=5734 (%)	MTAP intact (all) n=4936 (86.63%)	MTAP loss n=798 (13.37%)	p
N	5734	4936	798	
Age, median (IQR)	72.2 (9.13)	72.1 (9.13)	72.3 (8.98)	0.5545
Sex, n(%)				0.3726
Females	246 (4.29%)	217 (4.4%)	29 (3.63%)	
Male	5488 (95.71%)	4719 (95.6%)	769 (96.37%)	
Race				0.0747
Black or African American	1322 (23.06%)	1161 (23.52%)	161 (20.18%)	
White	4020 (70.11%)	3431 (69.51%)	589 (73.81%)	
Combined (American Indian or Alaska Native, Asian, Native Hawaiian or Other Pacific Islander)	102 (1.78%)	89 (1.8%)	13 (1.63%)	
Ethnicity				0.5609
Hispanic or Latino	150 (2.62%)	132 (2.67%)	18 (2.26%)	
Not Hispanic or Latino	5446 (94.98%)	4683 (94.87%)	763 (95.61%)	
Smoking history				0.3272
yes, n(%)	5462 (95.26%)	4695 (95.12%)	767 (96.12%)	
No, n(%)	257 (4.48%)	227 (4.6%)	30 (3.76%)	
NA	15 (0.26%)	14 (0.28%)	1 (0.13%)	
Smoking Type				0.562
Never, n(%)	257 (4.48%)	227 (4.6%)	30 (3.76%)	
Former, n(%)	3331 (58.09%)	2864 (58.02%)	467 (58.52%)	
Current, n(%)	2131 (37.16%)	1831 (37.09%)	300 (37.59%)	
NA	15 (0.26%)	14 (0.28%)	1 (0.13%)	
Histology				0.004541
Adenocarcinoma	3283 (57.25%)	2867 (58.08%)	416 (52.13%)	
Adenosquamous	65 (1.13%)	51 (1.03%)	14 (1.75%)	
Other NSCLC	528 (9.21%)	454 (9.2%)	74 (9.27%)	
Squamous cell carcinoma	1858 (32.4%)	1564 (31.69%)	294 (36.84%)	
Stage				0.7599
Stage I, n(%)	1141 (19.9%)	1010 (20.46%)	131 (16.42%)	
Stage II, n(%)	647 (11.28%)	557 (11.28%)	90 (11.28%)	
Stage III, n(%)	1278 (22.29%)	1093 (22.14%)	185 (23.18%)	
Stage IV, n(%)	2091 (36.47%)	1785 (36.16%)	306 (38.35%)	
Brain metastasis				0.6635
yes, n(%)	564 (9.84%)	481 (9.74%)	83 (10.4%)	
No, n(%)	4869 (84.91%)	4190 (84.89%)	679 (85.09%)	
Liver Metastasis				0.1264
yes, n(%)	420 (7.32%)	350 (7.09%)	70 (8.77%)	
No, n(%)	5022 (87.58%)	4327 (87.66%)	695 (87.09%)	

Table 1. Baseline Demographic and Clinical Characteristics of Patients Stratified by MTAP Status

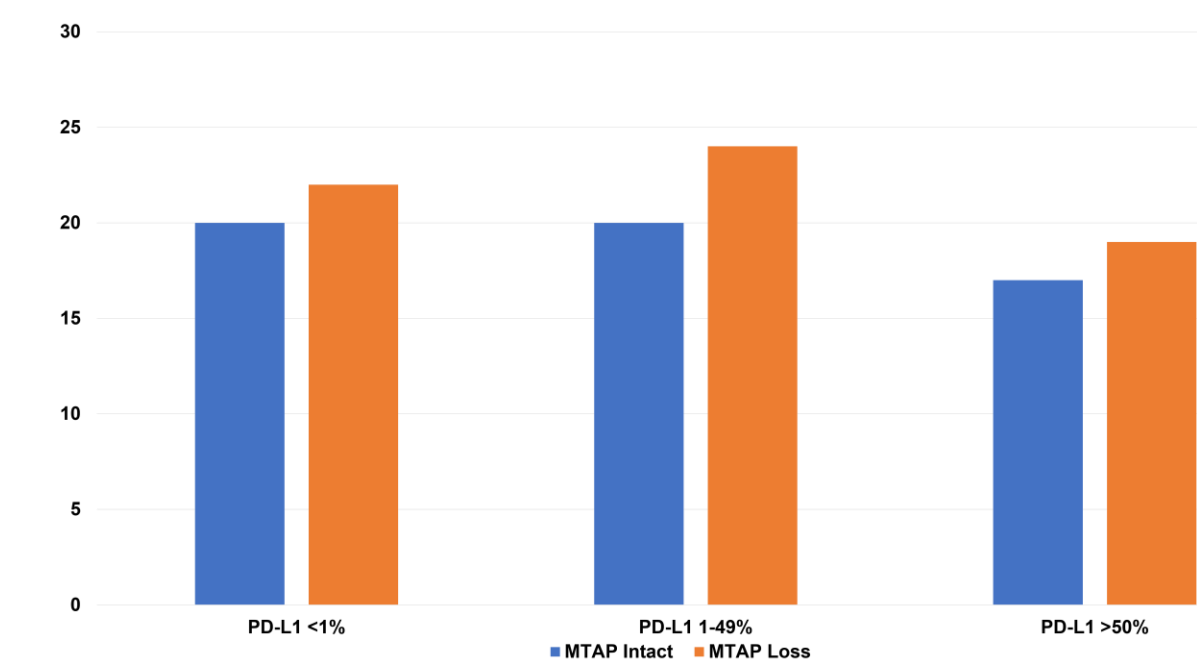


Figure 1: PD-L1 Expression (%) Stratified by MTAP Intact vs. MTAP Loss Status

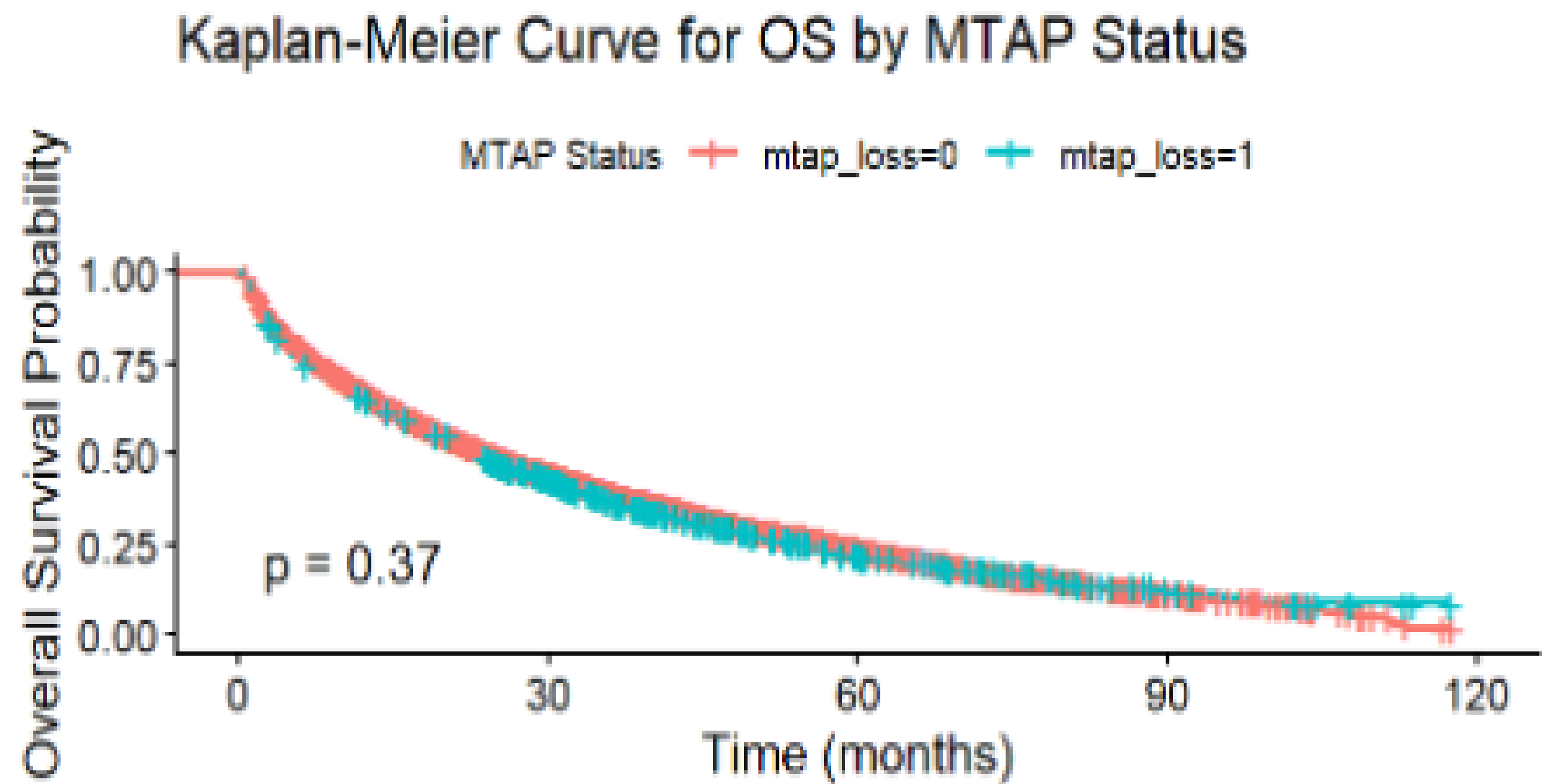


Figure 2: Kaplan-Meier Curve for OS by MTAP Status

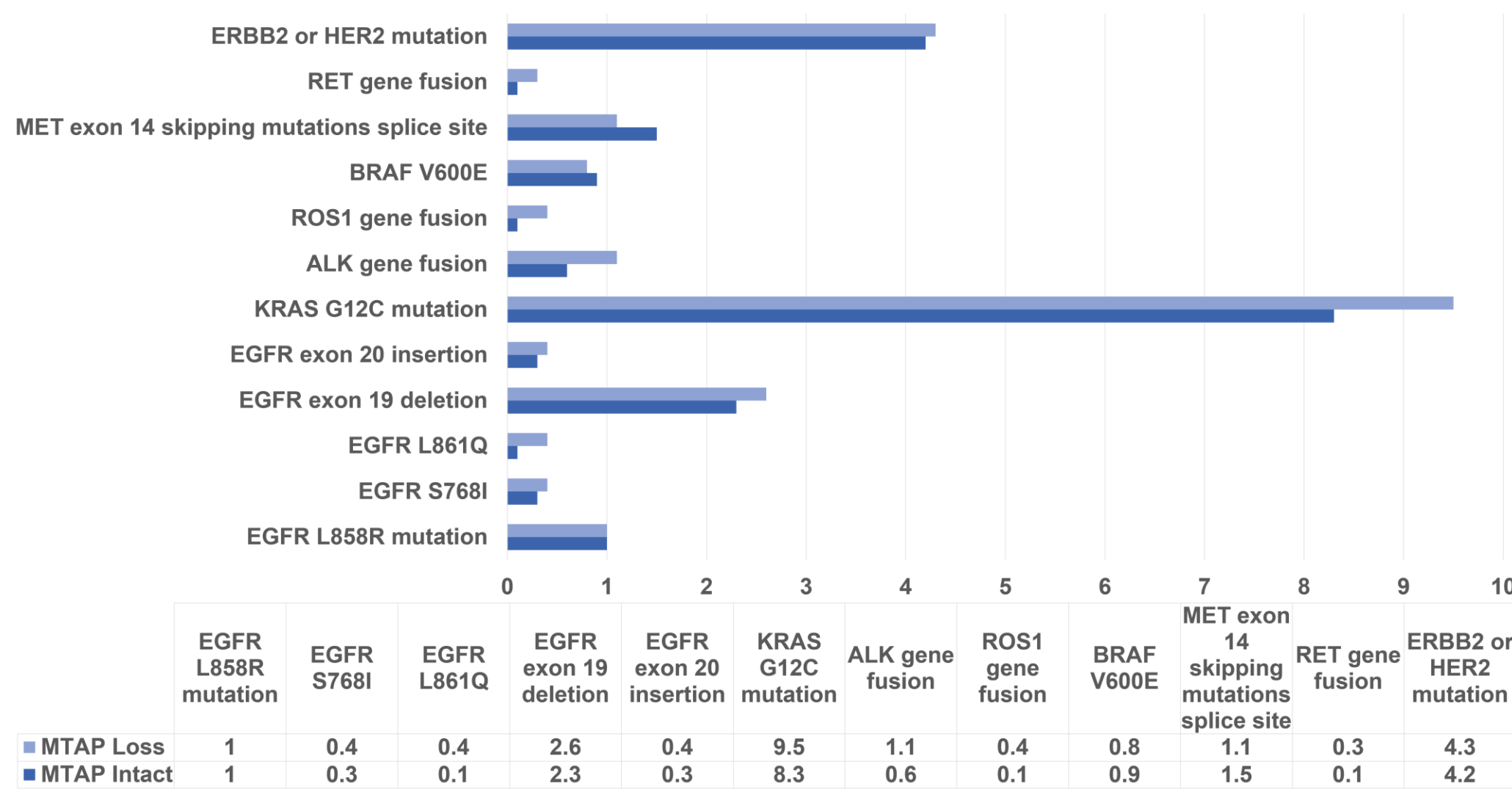


Figure 3: Frequency (%) of Common Oncogenic Driver Mutations in NSCLC, Stratified by MTAP Loss vs. MTAP Intact

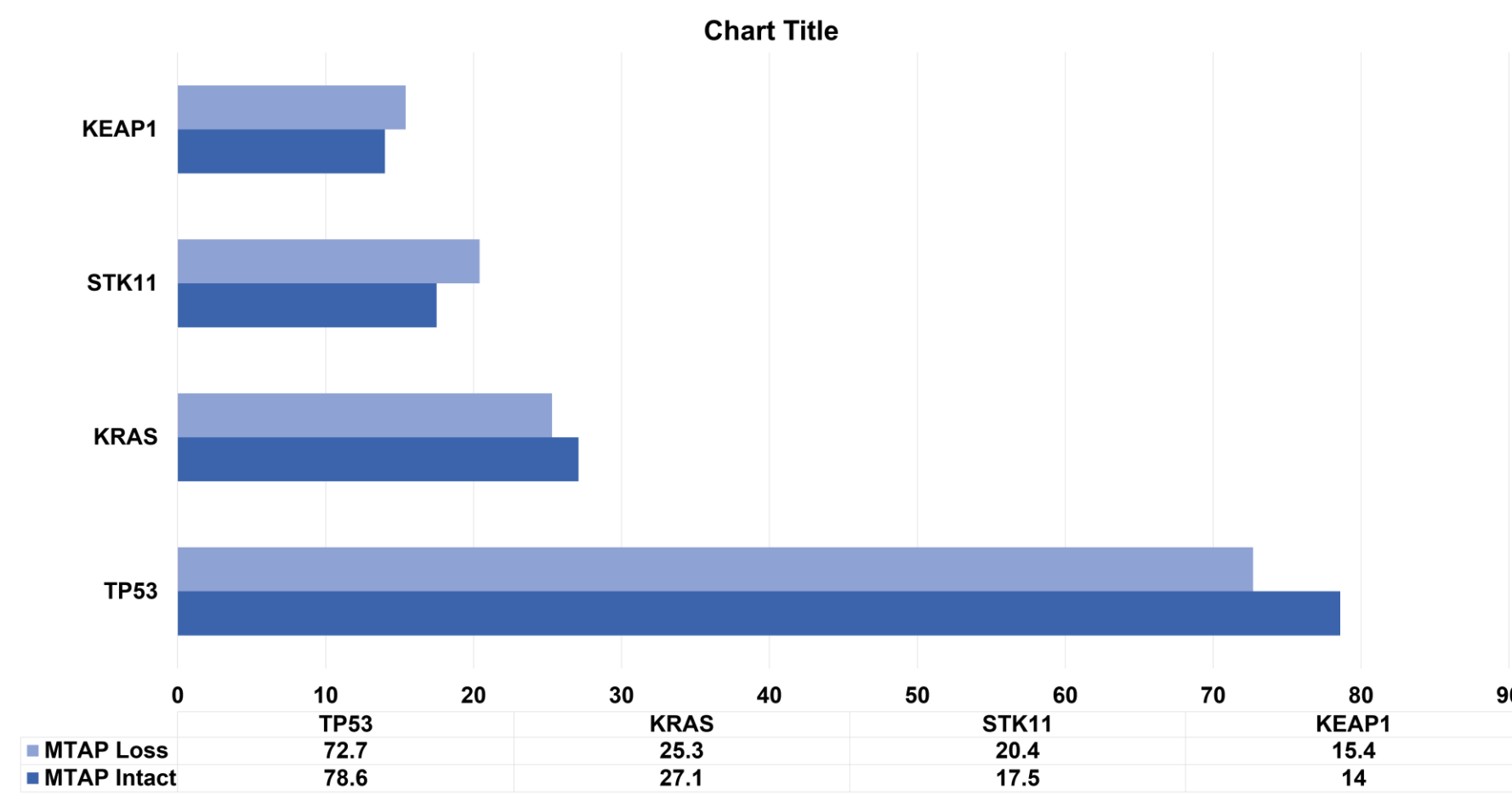


Figure 4: Prevalence of TP53, KRAS, STK11, and KEAP1 Mutations in MTAP Loss vs. MTAP Intact Tumors

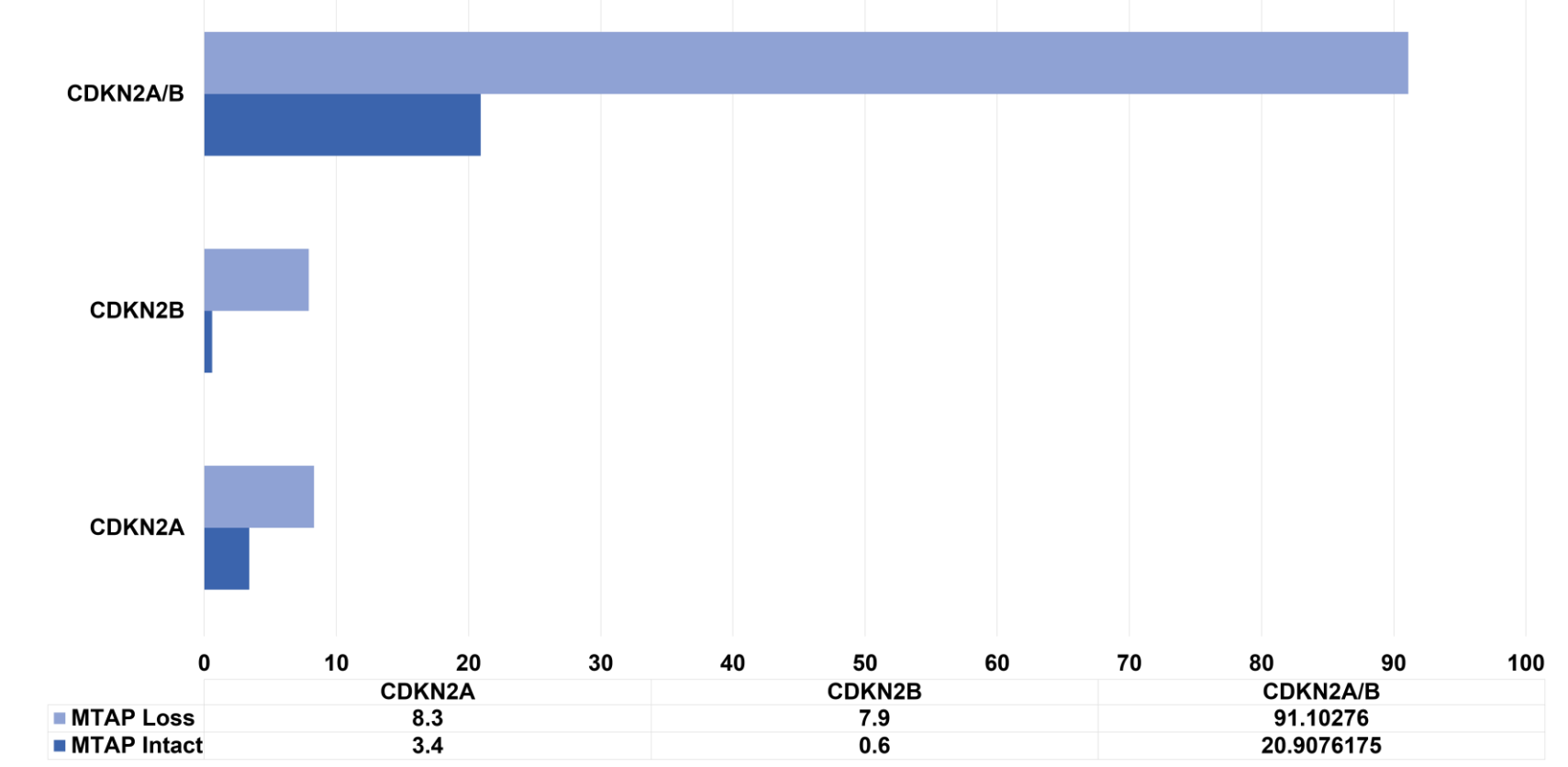


Figure 5: Frequency (%) of CDKN2A/B Co-deletion by MTAP Status