

INTRODUCTION

KRAS is among the most commonly mutated oncogenes in non-small cell lung carcinoma (NSCLC), with a higher prevalence in smokers. The advent of targeted therapies against the *KRAS* G12C mutation has led to significant clinical benefit, particularly when used in combination with other treatment modalities.in non-small cell lung carcinoma (NSCLC), with a higher prevalence in smokers. The advent of targeted therapies against the *KRAS* G12C mutation has led to significant clinical benefit, particularly when used in combination with other treatment modalities.

METHODS

- Retrospective review of lung cancer diagnosed at single urban medical center
- Cases confirmed with *KRAS* mutations identified by molecular profiling
 - KRAS* G12C vs non-G12C subgroups
- Histopathologic features and PD-L1 expression
 - high (>50%) or low (≤50%)
- Clinical data, including smoking status, were collected to evaluate associations with *KRAS* mutation subtype and tumor morphology

DISCUSSION AND CONCLUSION

- Take Away Points
- KRAS* G12C lung adenocarcinomas exhibit baseline clinical characteristics that are largely similar to non-G12C variants.
 - KRAS* G12C tumors show unique molecular and structural tendencies, favoring a higher frequency of TP53 co-mutations and higher nuclear grades, whereas non-G12C variants present more frequently with mucinous patterns.
 - This study provides critical insight into an underrepresented demographic, featuring a cohort that is 78% African American.
- Future Direction for Research
- Large-Cohort Validation: Expand the study to larger, multi-center cohorts to validate these molecular and histologic trends against a broader dataset.
 - Subtype Characterization: Continue deep molecular and clinical characterization of specific *KRAS* variants to better inform personalized treatment strategies.
 - Health Equity Research: Prioritize the inclusion of diverse populations to clarify potential race-specific tumor biology differences in *KRAS*-driven lung cancers.

REFERENCES & ACKNOWLEDGEMENTS

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RESULTS

Patient Cohort Demographics & Baseline Characteristics

- Among 41 total patients, 17 (41.5%) presented with *KRAS* G12C mutations and 24 (58.5%) presented with non-G12C *KRAS* mutations.
- Clinical stage at diagnosis was also comparable, with Stage 1 disease observed in 17.6% of G12C and 37.5% of non-G12C patients (p = 0.304 for Stage 1 vs. Stage 2–4).

Molecular & Histologic Profiles

- Co-mutation with TP53 was more frequent in G12C-mutated tumors (70.6% vs. 41.7%), though this did not reach statistical significance (p = 0.112).
- The non-G12C group more frequently exhibited high-grade patterns, specifically solid and papillary architecture, compared to the G12C group
- Additionally, liquid biopsy concordance rate was 57% and overall *KRAS* G12C positivity rate 10%.

Distribution of KRASGroup Across Stage Categories

Stage Category	G12C	nonG12C
1	3	9
2	2	2
3	4	2
4	8	11

Distribution of KRASGroup Across Stage Groups (1-2 vs 3-4)

Stage Group	G12C	nonG12C
Stage 1-2	5	11
Stage 3-4	12	13

	G12C mutated	non G12C mutated	p-value
Age_ Mean ± SD	61.8 ± 9.0	62.5 ± 7.7	
Age_Median (IQR)	63.0 (57.0-65.0)	62.5 (58.5-68.0)	0.787 **
Sex			
M	6 (35.3%)	7 (29.2%)	
F	11 (64.7%)	17 (70.8%)	0.742
Race			
African American	13 (76.5%)	19 (79.2%)	
Caucasian	2 (11.8%)	4 (16.7%)	
Hispanic	2 (11.8%)	1 (4.2%)	0.619
Stage			
1	3 (17.6%)	9 (37.5%)	
2	2 (11.8%)	2 (8.3%)	
3	4 (23.5%)	2 (8.3%)	
4	8 (47.1%)	11 (45.8%)	
Stage 1	3 (17.6%)	9 (37.5%)	
Stage 2-4	14 (82.4%)	15 (62.5%)	0.304
Stage 1-2	5 (29.4%)	11 (45.8%)	
Stage 3-4	12 (70.6%)	13 (54.2%)	0.641
Smoking			
Never	1 (5.9%)	2 (8.3%)	
Current	5 (29.4%)	10 (41.7%)	
Former	11 (64.7%)	12 (50.0%)	0.646
PD-L1(TPS)			
<50	12 (60.0%)	35 (70.0%)	
≥50	8 (40.0%)	15 (30.0%)	0.364
KRAS/TP53			
KRAS	5 (29.4%)	14 (58.3%)	
KRAS/TP53	12 (70.6%)	10 (41.7%)	0.112
Histomorphologic Evaluation of Cases with Available Slide			
	G12C mutated	non G12C mutated	p-value
KRAS/TP53			
KRAS	3 (25%)	13 (61.9%)	
KRAS/TP53	9 (75%)	8 (38.1%)	0.071
Nuclear Grade			
High	7 (58.3%)	8 (38.1%)	
Intermediate	2 (16.7%)	0 (0%)	
Low	3 (25%)	13 (61.9%)	0.042
Necrosis			
Yes	4 (33.3%)	4 (19%)	
No	8 (66.7%)	17 (81%)	0.64
Histopathologic Pattern			
Solid/Squamous	4 (33.3%)	7 (33.3%)	
Acinar and lepidic	4 (33.3%)	7 (33.3%)	
Papillary/Micropapillary	1 (8.3%)	4 (19%)	
Small cell	1 (8.3%)	0	
Adenosquamous	1 (8.3%)	0	
Mucinous	1 (8.3%)	3 (14.3%)	0.494

*Chi-square and Fisher's exact test used where appropriate.

**Normally assessed by Shapiro-Wilk; t-test or Mann-Whitney U applied as appropriate.