P1.207: Impact of *KRAS* mutations on Overall Survival in Lung Adenocarcinoma Patients Treated with Neoadjuvant Chemoimmunotherapy

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IASLC 2026 World Conference on Lung Cancer
SEPTEMBER 12 – 15, 2026
SEOUL, REPUBLIC OF KOREA

INTRODUCTION

Neoadjuvant chemotherapy combined with PD-(L)1 blockade (chemoimmunotherapy) has transformed the treatment landscape for resectable non-small cell lung cancer (NSCLC) (1-2).

The influence of *KRAS* oncogenic driver mutations on response to neoadjuvant chemoimmunotherapy and long-term outcomes remains poorly characterized (3).

Previous studies have described improved rates of pathological complete response after neoadjuvant chemoimmunotherapy in NSCLC *KRAS* mutated patients compared to *KRAS* wildtype patients (4-5).

No studies have assessed overall survival (OS) outcomes in neoadjuvant chemoimmunotherapy treated LUAD patients.

This study aims to evaluate differences in OS between lung adenocarcinoma (LUAD) patients with *KRAS* and other driver mutations following neoadjuvant and adjuvant chemoimmunotherapy.

METHODS

This retrospective study analyzed genomic, clinical and survival data.

Patients with stage IIA-IIIB LUAD treated with neoadjuvant chemoimmunotherapy, and LUAD stage IV patients treated with chemoimmunotherapy across three academic centers in Montreal, Canada were included.

Patients with *EGFR* or *ALK* mutations were excluded. Driver mutations were identified using the AmpliSeq Focus Panel.

The primary outcome was overall survival, compared between subgroups using the log-rank test.

RESULTS

79 stage IIA-IIIB and 53 stage IV LUAD patients were included.

In the neoadjuvant cohort, the median age was 68 (IQR 64-74), 63.3% (n = 50) were female, 97.5% (n = 77) were current or ex-smokers and 54.4% (n = 43) had stage III disease (Table 1). In the metastatic cohort, the median age was 64 (IQR 59-71) and 98% (n = 52) were current or ex-smokers.

In the neoadjuvant cohort, *KRAS*-mutated patients (n = 62) showed a trend toward improved OS compared to patients with non-KRAS mutations (*BRAF, MET, HRAS, ERRB2* and *PIK3CA*; n = 17) after neoadjuvant chemoimmunotherapy (p = 0.053) (Figure 1).

This difference reached statistical significance when restricted to *KRAS* G12C mutated patients (n = 28) versus those with other driver mutations (n = 17; p = 0.02) (Figure 2).

In contrast, no significant difference in OS was observed in the metastatic cohort between *KRAS*-mutated (n = 23) and non *KRAS*-mutated patients (n = 30; p = 0.31).

Variable	Level	KRAS (N = 62)	BRAF, MET, HRAS, ERBB2, PIK3CA (N = 17)
Sex	Male	24 (38.7)	5 (29.4)
	Female	38 (61.3)	12 (70.6)
Age, median [IQR]		68.00 [65.00, 74.00]	70.00 [59.00, 73.00]
Smoking Status	Never	1 (1.6)	1 (5.9)
	Ex-smoker	44 (71.0)	13 (76.5)
	Current	17 (27.4)	3 (17.6)
Clinical Stage	Stage II	26 (41.9)	10 (58.8)
	Stage III	36 (58.1)	7 (41.2)
Pathological Stage	Stage 0	11 (17.7)	2 (11.8)
	Stage I	20 (32.3)	6 (35.3)
	Stage II	22 (35.5)	2 (11.8)
	Stage III	9 (14.5)	5 (29.4)
	Stage IV	0 (0.0)	2 (11.8)
Pathologic Response	pCR	10 (33.3)	2 (28.6)
	MPR	20 (66.7)	5 (71.4)
DNA Variant	KRAS	62 (100)	0 (0.0)
	ERBB2	0 (0.0)	1 (5.9)
	H-Ras	0 (0.0)	1 (5.9)
	BRAF	0 (0.0)	3 (17.6)
	MET	0 (0.0)	7 (41.2)
	PIK3CA	0 (0.0)	5 (29.4)

Table 1. Demographic information for the neoadjuvant cohort.

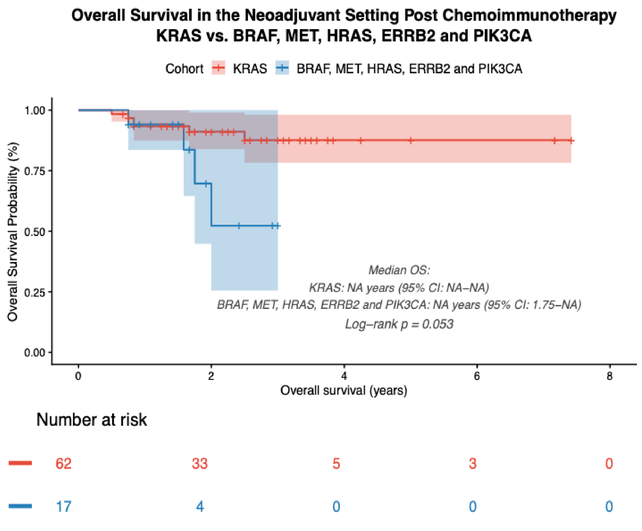


Figure 1. Overall survival in the neoadjuvant cohort (*KRAS* vs other)

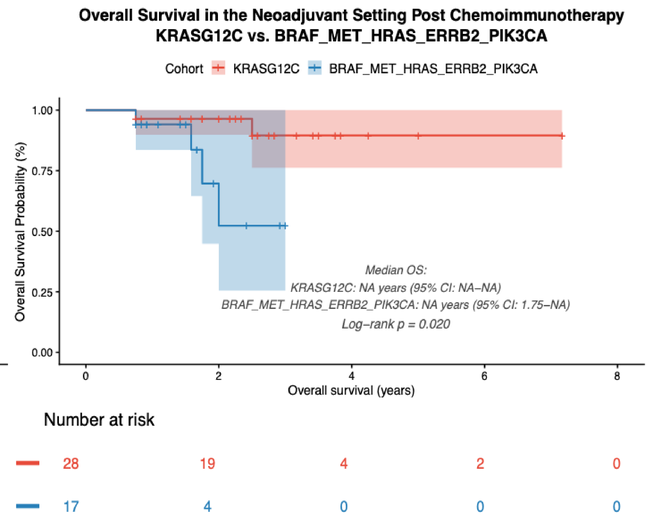


Figure 2. Overall survival in the neoadjuvant cohort (*KRAS* G12C vs other)

DISCUSSION AND CONCLUSION

KRAS G12C mutated LUAD patients demonstrated superior overall survival following neoadjuvant chemoimmunotherapy compared to patients harboring other driver mutations excluding *EGFR* and *ALK*.

These findings highlight the importance of mutation-specific treatment stratification in resectable LUAD and the need for novel neoadjuvant strategies for patients with less favorable outcomes.

Given the small sample sizes, our data remains exploratory and hypothesis generating.

Prospective studies with larger cohorts are needed to validate the prognostic and predictive role of specific driver mutations in LUAD patients receiving neoadjuvant chemoimmunotherapy.

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We thank all the patients and families who participated in this research and made this work possible. We also acknowledge the members of the Thoracic Clinical Trials Group at the McGill University Health Centre for their contributions to this research.