

EP: Targetable *RET*, *ALK*, and *ROS1* Fusions in Early-Stage NSCLC ≤ 30mm: A Real-World Analysis

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IASLC 2026 World
Conference on Lung Cancer

SEPTEMBER 12 - 15, 2026
SEOUL, REPUBLIC OF KOREA

INTRODUCTION

Targetable gene fusions involving *RET*, *ALK*, and *ROS1* define important therapeutic subsets of non-small cell lung cancer (NSCLC), yet their relevance in early-stage, small (≤30 mm) tumors remains unclear. Molecular testing is not uniformly performed in this setting, and the prevalence of actionable alterations in small, resected tumors is not well established. Results from the existing literature show even after resection, these cancers have a higher rate of recurrence. We sought to characterize the frequency and distribution of *RET*, *ALK*, and *ROS1* fusions in a real-world cohort of early-stage NSCLC and to examine their associations with smoking status, race, and survival patterns.

METHODS

We analyzed data from the Initiative for Early Lung Cancer Research on Treatment (IELCART), a prospective, multi-institutional cohort study initiated in 2016, including patients undergoing surgical resection for lung tumors TNM 9th edition, clinical stage IA (≤30mm) with available molecular profiling. Tumors were evaluated for *RET*, *ALK*, and *ROS1* fusions, and fusion-positive cases were identified and compared with non-fusion cases. Radiological, clinical, and demographic characteristics, including race and smoking status, as well as outcomes, were assessed. Descriptive analyses were performed.

Continuous variables were summarized using medians and interquartile ranges (IQRs), and categorical variables were summarized using frequencies and percentages. Patient, tumor, surgical, and pathologic characteristics were compared across *RET*, *ALK*, *ROS1* fusion group and non-fusion groups. The Kruskal–Wallis test was used for comparisons of continuous variables, and the chi-square test or Fisher's exact test, as appropriate, was used for categorical variables.

Molecular testing reports were abstracted from the patient electronic medical records. Each report had a corresponding pathology report from a biopsy or surgical resection or from an independent blood draw. The molecular testing was conducted by laboratories from the Molecular Pathology Laboratory (Mount Sinai Medical Center), Sema4 Genomics, Caris Life Sciences, Foundation Medicine, and Guardant Health.

DISCUSSION AND CONCLUSION

Fusion drivers potentially contribute to a rise in lung cancer for patients who are younger and who have never smoked cigarettes

- Post-surgical outcomes and survival in patients with lung cancers caused by fusion drivers appeared favorable and consistent with those undergoing surgery for early-stage NSCLC
- Early detection of lung cancer, regardless of detected molecular alteration, remains the key to having the best survival and curability for lung cancer
- These findings highlight the possibility of these patients being excluded from lung cancer screening eligibility guidelines, and the need to screen younger patients, and those who have never smoked

Future direction for research

- Longer term follow-up on patients with detected fusion drivers to better understand survival and recurrence outcomes, compared to the general study population
- Further explore the effect of these molecular alterations in stage I lung cancers and how the treatment paradigm changes compared to the standard of care

REFERENCES & ACKNOWLEDGEMENTS

- Cohn Vizitiu, Ester-Andreea; Tataru, Ecaterina; Csutak, Ortansa. Comprehensive molecular diagnostic tests in non-small cell lung cancer: frequency of *ALK*, *ROS1*, *RET*, and other gene fusions/rearrangements in a Romanian cohort. *Cancers (Basel)* 2025; 17(22):3673.
- Takeuchi, Kengo; Soda, Manabu; Togashi, Yuki, et al. *RET*, *ROS1* and *ALK* fusions in lung cancer. *Nature Medicine* 2012; 18(3):378-381.

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*Google Gemini was used to create Figure 1. The data was inputted by the author.

The research was supported by generous grants from the Simons Foundation (International Ltd.). These sponsors had no involvement in the study design, data collection, analyses, interpretation of the data, or in the creation of this poster.

We would like to thank all of the participants of the Initiative for Early Lung Cancer Research on Treatment study.

RESULTS

- Among 514 patients with molecular profiling, we identified 17 (3.3%) patients with a *RET*, *ALK*, or *ROS1* fusion. There were 8 (1.5%) *ALK*, 6 (1.2%) *ROS1*, and 3 (0.6%) *RET* fusions.
- Patients with a fusion driver were younger (62 vs 71; p<0.001), more likely to be a person who never smoked (65% vs 24%; p=0.002), and less likely to have COPD (0% vs 21%; p=0.03) than a patient with a non-fusion oncogenic driver.
- Lung cancers from patients with a fusion driver were more likely to be located in the lower lobes (53% vs 29%; p=0.037) and less likely to be adenocarcinoma (82% vs 94%; p=0.014) compared to patients with a non-fusion oncogenic driver.
- After adjusting for age, sex, smoking status, smoking pack-years, and nodule size, there were no significant differences in either overall survival or lung cancer-specific survival between patients with *RET*, *ALK* or *ROS1* fusion and those with a different oncogenic driver.

Fusion-Positive Case Distribution (N=17)

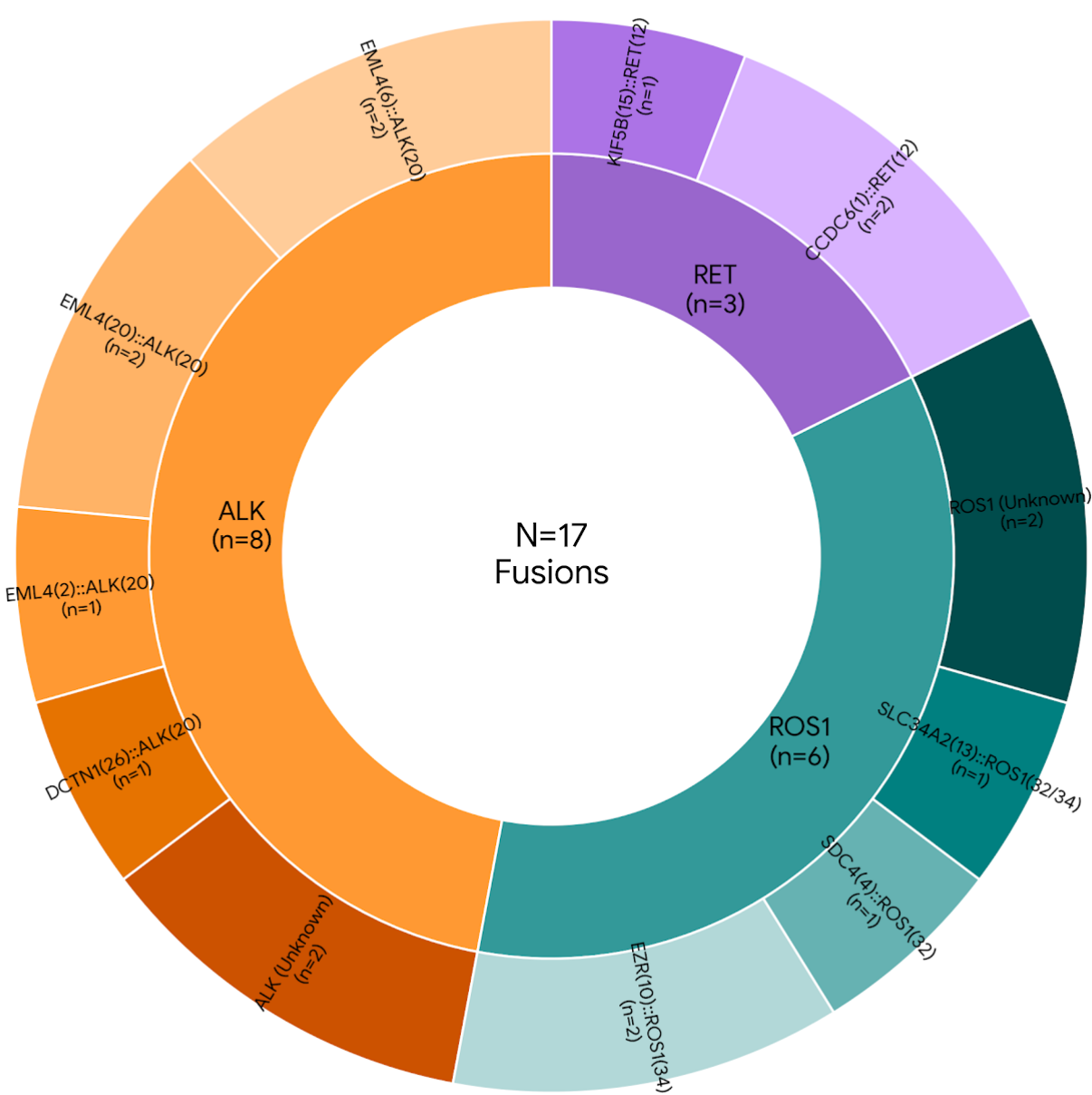


Figure 1. Fusion-positive case distribution

Characteristic	Overall N = 514 ¹	Fusion N = 17 ¹	Non-Fusion N = 497 ¹	p-value ²
Nodule Consistency				0.3
Non-solid	37 (7.2%)	1 (5.9%)	36 (7.3%)	
Part-solid	108 (21%)	1 (5.9%)	107 (22%)	
Solid	368 (72%)	15 (88%)	353 (71%)	
Nodule size (mm), median (IQR)	15 (11 - 21)	17 (11 - 22)	15 (11 - 21)	0.5
Nodule Location				0.039
Lower lobes	156 (30%)	9 (53%)	147 (29%)	
Upper/Middle lobes	358 (70%)	8 (47%)	350 (71%)	
Surgery Approach				0.8
Robotic-Assisted	68 (13%)	3 (18%)	65 (13%)	
Thoracotomy	87 (17%)	2 (12%)	85 (17%)	
VATS	359 (70%)	12 (71%)	347 (70%)	
Surgical Extent				0.6
Bilobectomy	3 (0.6%)	0 (0%)	3 (0.6%)	
Lobectomy	179 (35%)	8 (47%)	171 (35%)	
Other	1 (0.2%)	0 (0%)	1 (0.2%)	
Segmentectomy	31 (6.0%)	0 (0%)	31 (6.2%)	
Wedge Resection	300 (58%)	9 (53%)	291 (58%)	
Size of resected tumors (mm)	18 (13 - 22)	20 (14 - 25)	18 (13 - 22)	0.4
Histology				0.009
Adenocarcinoma	483 (94%)	14 (82%)	469 (94%)	
Other	12 (2.3%)	3 (18%)	9 (1.8%)	
Squamous Cell	19 (3.7%)	0 (0%)	19 (3.8%)	
Angiolymphatic Invasion	181 (35%)	7 (41%)	174 (35%)	0.6
Vascular Invasion	23 (4.5%)	0 (0%)	23 (4.6%)	>0.9
Margin (mm)	15 (10 - 25)	15 (10 - 35)	15 (10 - 25)	0.4

¹n (%); Median (Q1 - Q3)

²Fisher's exact test; Wilcoxon rank sum test; Pearson's Chi-squared test

Table 2. Comparison of primary tumor characteristics

Characteristic	Overall N = 514 ¹	Fusion N = 17 ¹	Non-Fusion N = 498 ¹	p-value ²
Age, median (IQR)	71 (64 - 77)	62 (55 - 72)	71 (65 - 77)	<0.001
Sex				0.4
Female	297 (58%)	8 (47%)	289 (58%)	
Male	217 (42%)	9 (53%)	208 (42%)	
BMI	25.7 (22.7 - 29.6)	26.9 (24.0 - 28.3)	25.7 (22.7 - 29.6)	0.8
Race				0.3
Black or African American	72 (14%)	1 (6%)	71 (14%)	
Asian	69 (13%)	4 (24%)	65 (13%)	
Others	55 (11%)	3 (18%)	52 (10%)	
White	317 (62%)	9 (53%)	308 (62%)	
Ethnicity				0.7
Hispanic or Latino	75 (15%)	3 (18%)	72 (14%)	
Not Hispanic or Latino	439 (85%)	14 (82%)	425 (86%)	
Smoking Status				0.002
Current	58 (11%)	1 (6%)	57 (11%)	
Former	328 (64%)	5 (29%)	323 (65%)	
Never	128 (25%)	11 (65%)	117 (24%)	
Pack-years among smokers, median (IQR)	30 (13 - 48)	15 (5 - 33)	30 (13 - 48)	0.10
Cardiac	75 (15%)	2 (12%)	73 (15%)	>0.9
Hypertension	254 (49%)	6 (35%)	248 (50%)	0.2
COPD	105 (20%)	0 (0%)	105 (21%)	0.030
Diabetes	87 (17%)	0 (0%)	87 (18%)	0.091
Family history of lung cancer				0.7
None	423 (82%)	15 (88%)	408 (82%)	
Yes	91 (18%)	2 (12%)	89 (18%)	

¹Median (Q1 - Q3); n (%)

²Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

Table 1. Baseline characteristics and self-reported comorbidities

	Fusion3	Non-Fusion
Urologic	17.6%	16.1%
Pulmonary	0.0%	6.2%
Neurology	0.0%	1.8%
Miscellaneous	0.0%	0.8%
Infections	5.9%	0.8%
Hematology	0.0%	1.0%
Gastrointestinal	0.0%	0.2%
Cardiovascular	5.9%	6.8%

Figure 2. Comparison of postoperative outcomes and complications