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The frequency of driver alterations in non-small cell lung cancer patients: Slovenian nationwide observational cohort trial

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INTRODUCTION

Next-generation sequencing (NGS) biomarker testing is recommended for all patients with advanced non-small cell lung cancer (NSCLC).

In Slovenia, reflex and routine NGS testing was introduced in 2022 for **all newly diagnosed non-squamous NSCLC (non-sq NSCLC) cases,** regardless of disease stage.

More than 90% of all samples are analyzed in a single national laboratory (approximately 800–900 samples per year).

This study provides the **first comprehensive analysis of genetic biomarkers in Slovenian non- sq NSCLC patients.**

1 METHODS

Initial biopsies from non-squamous NSCLC patients were collected between January 2022 and December 2024. A total of 2,559 patients were tested during the study period, with a mean age of 70 years (min. 31, max. 96 years); 52 % were male.

NGS was performed on all samples using the Thermo Fisher Oncomine Precision Assay on the Genexus® System. The study reports the frequency and distribution of actionable oncogenic drivers, stratified by subgroups, age, and sex.

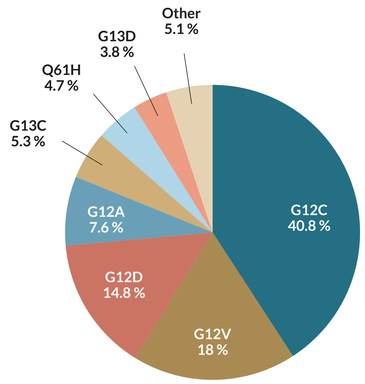
2 RESULTS

Targetable driver alterations were detected in 1504 (59 %) samples. The overall frequencies are summarized in Table 1, while detailed distributions of KRAS and EGFR variants are presented in Figures 1 and 2, respectively.

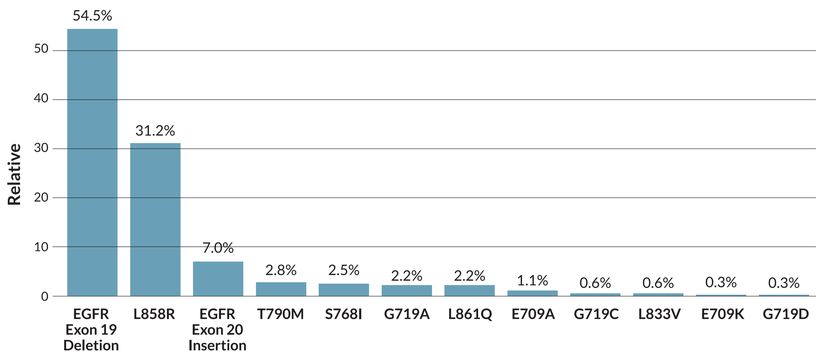
Frequency of targetable driver alterations was higher in women (67 % vs. 52 %), with distinct mutation patterns illustrated in Table 2. No significant differences in the frequency of driver alterations were observed between patients younger than 50 years and those aged 50 years or older (60 % vs 59 %).

Gene	N (%)
KRAS mutation	922 (36.03 %)
EGFR mutation	356 (13.91 %)
ALK fusion	74 (2.89 %)
BRAF V600E	42 (1.64 %)
MET Ex14 Skipping mutation	42 (1.64 %)
RET fusion	32 (1.25 %)
ROS1 fusion	17 (0.66 %)
ERBB2 mutation	16 (0.63 %)
NRG1 fusion	8 (0.31 %)
NTRK 1/2/3 fusion	1 (0.04 %)

◀◀ *Table 1:*
Frequency of targetable driver alterations in 2,559 Slovenian non-squamous NSCLC patients.



◀ *Figure 1:*
Prevalence/Frequencies of KRAS mutations. Molecular analysis covers actionable alterations within codons 12, 13, 59, 61, and 146 of the KRAS gene. Group "Other" comprises all other detected KRAS mutations.



◀ *Figure 2:*
Frequency of detected variants of the EGFR gene. Molecular analysis involves common and rare alterations within exons 18, 19, 20, and 21 of the EGFR gene.

	SEX		AGE	
	M	F	>50 years	<50 years
Frequency of all targetable driver alterations	698 (52 %)	806 (67 %)	1469 (59 %)	35 (60 %)
ALK fusion	31 (2.30 %)	43 (3.56 %)	66 (2.63 %)	8 (16.33 %)
BRAF V600E	15 (1.11 %)	27 (2.23 %)	42 (1.67 %)	0 (0.0 %)
EGFR mutation	104 (7.7 %)	252 (20.84 %)	353 (14.06 %)	3 (6.12 %)
ERBB2 mutation	9 (0.67 %)	7 (0.58 %)	16 (0.64 %)	0 (0.0 %)
KRAS mutation	494 (36.59 %)	428 (35.40 %)	911 (36.29 %)	11 (22.45 %)
MET Ex14 Skipping mutation	18 (1.33 %)	24 (1.99 %)	42 (1.67 %)	0 (0.0 %)
NRG1 fusion	3 (0.22 %)	5 (0.41 %)	8 (0.32 %)	0 (0.0 %)
NTRK 1/2/3 fusion	1 (0.07 %)	0 (0.0 %)	1 (0.04 %)	0 (0.0 %)
RET fusion	16 (1.19 %)	16 (1.32 %)	30 (1.20 %)	2 (4.08 %)
ROS1 fusion	9 (0.67 %)	8 (0.66 %)	13 (0.52 %)	4 (8.16 %)

◀ *Table 2:*
Prevalence and distribution of driver mutations according to sex and age

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Katja Mohorčič has no conflicts of interest to declare

CONCLUSIONS

The frequency and distribution of driver alterations in Slovenian non-squamous NSCLC patients are broadly comparable to those reported in other European populations.

A higher prevalence was observed among females, while no significant differences were detected between patients aged ≤ 50 years and those older than 50 years.