

Lung Cancer Spectrum, Molecular Alterations and PD-L1 Expression

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Abstract

Aim

This audit evaluated lung cancer cases diagnosed in 2024, focusing on histological subtypes, molecular testing, and PD-L1 expression to assess diagnostic trends and biomarker testing compliance.

Methods

All lung malignancy cases on core biopsy or cytology between January 1 and December 31, 2024, were included. Data were extracted from the institutional lab information system (Win-Path and Power-chart).

Results

Adenocarcinoma was the most common subtype, accounting for 91 (55%) cases, followed by squamous cell carcinoma 32 (19%) cases, small cell carcinoma, 17 (10%) cases, carcinoma NOS, 24 (14%) cases, and High-grade Neuroendocrine carcinoma, 1 (1%) case. Molecular testing was performed in 83 (50%) cases. Reflex testing by pathologists was done in 76 (92%) cases and testing was done on clinician's request in 7 (8%) cases. Mutations were identified in 38 (46%) cases of them. KRAS mutations were detected in 19 (50%), EGFR in 8 (21%), BRAF in 6 (16%), MET exon 14 skipping in 2 (5%), and PIK3CA in 3 (8%). PD-L1 immunohistochemistry was performed on 110 (66%) of total cases. Among these, the tumour proportion score was <1% in 50 (45.5%) cases, 1–49% in 28 (25.5%) cases, and ≥50% in 32 (29%) cases.

Discussion

Adenocarcinoma predominated, KRAS was the most common driver mutation, and PD-L1 expression influenced treatment decisions, aligning with global trends in precision oncology.

Introduction

Lung cancer remains one of the most common and deadliest cancers in Ireland. According to the National Cancer Registry Ireland (NCRI), there were roughly 2,700 new lung cancer diagnoses in the most recent reporting period and lung cancer accounts for about one in five cancer deaths nationally^{8–10}. Age-standardised incidence also shows regional variation: the NCRI reports a national rate of about 64 per 100,000 population with a higher rate in the Dublin & North-Midlands area (DNML) of 74 per 100,000, indicating a greater local burden in our catchment compared with the national average^{8–9}. Importantly, Ireland has recently moved to piloting targeted low-dose CT lung screening (the Beaumont RCSI / Irish Cancer Society “Lung Health Check” pilot and related national screening evaluation work supported by the National Screening Service)^{11–14}, and these organised screening programmes — supported by international trial evidence that low-dose CT screening increases early detection and reduces lung-cancer mortality [NLST¹⁵, NELSON¹⁶ and other related trials] — are expected to increase the number of lung cancers detected (particularly early-stage disease) in the coming months to years. These epidemiologic and screening developments provide the context for this 2024 audit of histopathology, molecular testing, and PD-L1 reporting across core biopsy and cytology specimens in our institute.

This audit was conducted to evaluate the spectrum of lung cancer cases diagnosed in the year 2024, with special emphasis on histological subtypes, frequency, molecular testing, and PD-L1 expression. The data was collected from all histopathology and cytology samples received during the study period. The objective was to assess diagnostic trends, molecular profiling practices, and biomarker testing compliance, and to identify areas for improvement in lung cancer diagnostic workflows.

Methods

All cases diagnosed as lung malignancies on core biopsy or cytology between January 1, 2024, and December 31, 2024, were included. Data was extracted from the institutional lab information system (Win-Path and Power-chart).

The following parameters were analysed:

- Number of tumour cases (core biopsies and cytology cases)
- Types of tumours
- Frequency of each tumour type
- Molecular testing (performed or not)
- Identified mutations/fusions
- PD-L1 done or not and its tumour proportion score (TPS)

Histological classification was based on WHO Classification of Thoracic Tumours (5th Edition, 2021)¹. Molecular tests included checking mutations in DNA for EGFR, BRAF, KRAS, ERBB2 and PIK3CA, checking fusions in RNA for ALK, ROS1, NTRK and RET, checking for MET exon 14 skipping. PD-L1 expression was assessed using immunohistochemistry and reported as Tumour Proportion Score (TPS)⁴.

Results

A total of 166 lung cancer cases were diagnosed in 2024, comprising 89 histopathology specimens (84 core biopsies, 3 CT-guided core biopsies and 2 transbronchial biopsies) and 77 cytology specimens (74 EBUS and 3 washings). Adenocarcinoma was the most common tumour subtype, accounting for (91 cases; 55%), followed by squamous cell carcinoma (32 cases; 19%), small cell carcinoma (17 cases; 10%), mixed small cell and large cell neuroendocrine carcinoma (1 case, less than 1%) and carcinoma NOS (24 cases; 14%). Metastatic carcinoma were excluded from the study.

Molecular testing was performed in 83 cases (50%). Out of these, reflex testing by pathologists was done in 76 cases (92%) and testing was done on clinician's request in 7 cases (8%). Mutations were identified in 38 cases (46%) of them. KRAS mutations were detected in 19 (50%), EGFR in 8 (21%), BRAF in 6 (16%), MET exon 14 skipping in 2 (5%), and PIK3CA in 3 (8%).

Of the adenocarcinomas tested, 35 cases showed an identifiable mutation or fusion. No mutations were detected in the two squamous cell carcinoma samples tested, and molecular testing was not performed for small cell or mixed neuroendocrine carcinoma. Among carcinoma NOS, 3 cases showed a detectable alteration.

Across all tumour types, the most frequent molecular alteration was KRAS, occurring in 19 adenocarcinoma cases and 1 carcinoma NOS case. EGFR mutations were identified in 8 adenocarcinoma cases, while BRAF mutations were found in 6 adenocarcinoma cases. MET exon 14 skipping mutations were detected in 2 adenocarcinoma cases and PIK3CA mutations were observed in 1 adenocarcinoma case and 2 cases of carcinoma NOS.

PD-L1 immunohistochemistry was performed on 110 (66%) of total cases. Among these, the tumour proportion score was <1% in 50 cases (45.5%), 1–49% in 28 cases (25.5%), and ≥50% in 32 cases (29%). PD-L1 immunohistochemistry was performed on 72 adenocarcinoma, 25 squamous cell carcinoma, 14 carcinoma NOS. Among adenocarcinomas, 33 (46%) had TPS <1%, 18 (25%) had TPS 1–49%, 20 (28%) had TPS ≥50%, and 1 sample had insufficient material. In squamous cell carcinoma, 13 cases (52%) had TPS <1%, 4 (16%) had TPS 1–49%, 6 (24%)

had TPS $\geq 50\%$, and 2 samples had insufficient material. For carcinoma NOS, 3 cases (21%) had TPS $< 1\%$, 6 (43%) had TPS 1–49%, and 5 (36%) had TPS $\geq 50\%$.

Table 1: Distribution of Tumour Types

Tumour Type	No. of Cases	Percentage (%)
Adenocarcinoma	91	55%
Squamous cell carcinoma	32	19%
Small cell carcinoma	17	10%
Carcinoma NOS	24	14%
Mixed small cell and large cell neuroendocrine carcinoma	1	Less than 1%

Table 2: Molecular Testing

Tumour Type	Molecular Test Done	Mutation/Fusion Identified
Adenocarcinoma	63 cases	35 cases (56%)
Squamous cell carcinoma	2 cases	No mutations identified.
Small cell carcinoma	Not done	Not applicable
Mixed small cell and large cell neuroendocrine carcinoma	Not done	Not applicable
Carcinoma NOS	14 cases	3 cases (21%)

Table 3: Summary of Molecular Findings

Tumour Type Involved	Molecular Alteration	No. of Positive Cases
Adenocarcinoma	EGFR mutation	8
Adenocarcinoma	KRAS mutation	18
Adenocarcinoma	BRAF mutation	6
Adenocarcinoma	Met exon 14 skipping mutation	2
Adenocarcinoma	PIK3CA mutation	1
Carcinoma NOS	KRAS mutation	1
Carcinoma NOS	PIK3CA mutation	2

Table 4: PD-L1 Expression (Tumour Proportion Score)

Tumour Type	No. Tested	TPS <1%	TPS 1–49%	TPS ≥50%
Adenocarcinoma	72	33	18	20
Squamous cell carcinoma	25	13	4	6
Small cell carcinoma and mixed large and small neuroendocrine carcinoma	0	N/A	N/A	N/A
Carcinoma NOS	14	2	6	5

Discussion

EGFR mutation status is critical when evaluating patients with a view to placing them on EGFR Tyrosine Kinase Inhibitors (TKIs). The presence of a sensitising mutation is associated with a favourable response to treatment with EGFR Tyrosine Kinase Inhibitors (TKIs)³. The presence of resistance mutations are not associated with a favourable response to treatment with EGFR Tyrosine Kinase Inhibitors (TKIs)³. Specific KRAS G12C inhibitors have been shown to be effective in the treatment of patients with KRAS G12C mutant non-small cell lung cancer^{5–7}.

The presence of a BRAF V600 variant has been shown to be associated with a response to treatment with BRAF-targeted therapies in combination with MEK1/2 targeted inhibitor⁶. There are currently no approved treatment options for lung cancer patients with ERBB2 exon 20 in-frame insertions. There are a number of actively recruiting clinical trials⁵. There are currently no approved treatment options for lung cancer patients with PIK3CA mutations⁵.

This audit provides an overview of lung cancer tumour types and molecular profiling at our institution for the year 2024. Preliminary analysis suggests that adenocarcinoma was the predominant subtype accounting for 53% of cases. KRAS was the most common driver mutation detected, followed by EGFR and BRAF. PD-L1 immunohistochemistry was performed on 110(66%) of cases. Its expression distribution was TPS <1% = 50(45.5%), TPS 1–49% = 28(25.5%), TPS ≥50% = 32(29%). PD-L1 expression results subsequently had implications on treatment decisions. The results align broadly with global trends, where adenocarcinoma represents the most frequent histological subtype and molecular profiling is crucial for targeted therapy selection^{2,5–7}. Regular audits of molecular testing ensure adherence to international guidelines and support precision oncology initiatives³.

Declarations of Conflicts of Interest:

None declared.

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