Characterization of Patients with Lung Cancer Not Meeting Lung Cancer Screening Criteria: Identifying a High-Risk Group Beyond Tobacco Smoking

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BACKGROUND

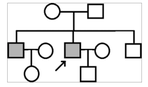
- **Lung cancer screening** (LCS) programmes, based mainly on age and smoking history, have demonstrated a significant reduction in lung cancer (LC) mortality, prompting their gradual adoption[1-2]
- However, **up to 40% of LC cases occured in patients LCS-ineligible** according current LCS criteria.
- **Susceptibility factors** reflected by family and personal history of cancer (FHC, PHC), could help to identify a **high-risk population**, not considered currently in LCS programmes.

OBJECTIVE:

To characterize the clinical and tumor profiles, as well as familial and individual susceptibility in patients with NSCLC who didn't meet LCS criteria

METHODS

- **Prospective study** of 350 patients with **all-stages NSCLC** treated at Hospital Clinic of Barcelona (Spain) between Oct/2020 to Jan/2025.
- Patients had a **personal interview** to collect personal and family history of cancer (three-generation pedigree), demographic data, and exposure to environmental and occupational carcinogens. Clinical and molecular data was collected from medical records.



- Patients were classified as **LCS-eligible or ineligible at the time of NSCLC diagnosis** according to Nelson criteria [who had quit ≤10 years ago] who had smoked (50-74 years old (yo) current or former smokers >15 cigarettes a day for >25 years or >10 cigarettes a day for >30 years).
- The patient/tumor/family profile was analyzed in each LCS-ineligible group and compared with LCS-eligible patients.

RESULTS

Study population

Baseline characteristics N=350 (%)		
Age	Median, range	65 (30-88)
Gender	Male	201 (57)
	Female	149 (43)
Smoking status	Ever-smokers	289 (83)
	Non-smokers	61 (17)
Histology	Adenocarcinoma	255 (72)
	Squamous	51 (15)
	Others	44 (13)
Stage	Stage IV	187 (54)
	Stage I-III	161 (46)
PDL1 status	≤1%	117 (33)
	1-49%	96 (27)
	≥50%	91 (26)
	No data	46 (13)
Molecular status	Driver*	242 (74)
	No Driver	98 (28)
	Missing	12 (3)

Table 1. Baseline characteristics

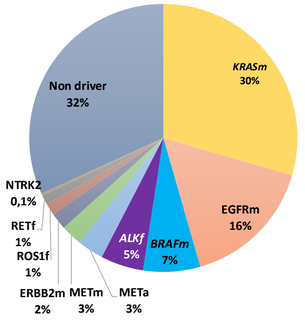
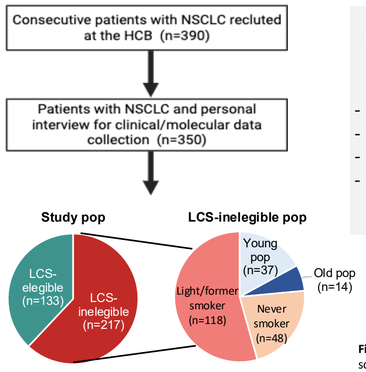


Figure 1. Distribution of the study population by molecular status.

*Driver population was defined as somatic mutations (m) in *EGFR/KRAS/BRAF/MET/ERBB2*, fusions (f) in *ALK/ROS1/RET/NTRK1-3*, amplifications (a) in *ERBB2/MET*

LCS-inelegible population



Out of 350 patients, **217 (62%) didn't meet LCS criteria** due to:

- Young age at NSCLC diagnosis (17%)
- Old age at NSCLC diagnosis (6%)
- Never-smoking status (22%)
- Low tobacco exposure (54%)

Figure 2. Flowchart of the study. LCS: Lung cancer screening; pop: population

Family & Personal History of Cancer in the LCS-inelegible population

Family History of Cancer

The prevalence of 1st-degree affected relatives was similar in both groups.

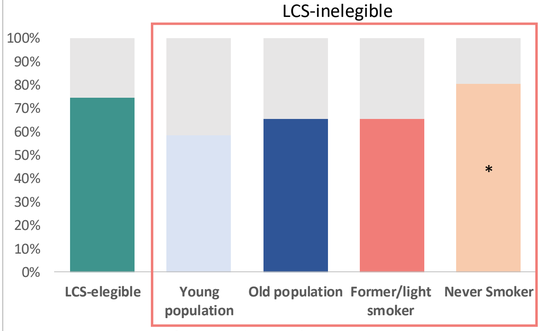


Figure 3. Proportion of patients with FHC in 1st-degree relatives by subgroup.

* By subgroup, the LCS-ineligible group due to non-smoking status showed the highest rate of FHC (82%), particularly colorectal (20%), breast (18%), and lung (12%) cancers.

Personal History of Cancer

- PHC was most common among LCS-inelegible patients

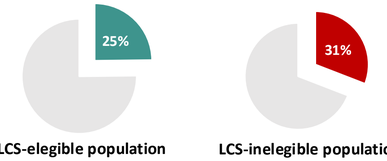


Figure 4. Proportion of patients with PHC in LCS-elegible and ineligible patients.

Tumor spectrum in the LCS-ineligible population by sex

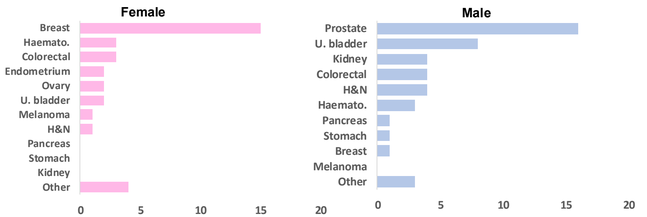


Figure 5. Cancer cases in patients from the LCS-ineligible group by sex. Haemato: Hamelatologic; H&N: Head and neck; U: urinary

Clinical & Molecular profile in LCS-inelegible population

A different profile was observed between LCS-ineligible and LCS-eligible populations, with a higher prevalence of female, lung adenocarcinoma, and driver alterations in the LCS-inelegible patients (p<0.001).

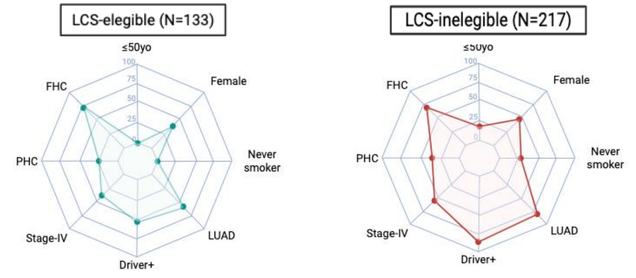


Figure 6. Radar plot with clinical/molecular profile in LCS-elegible and LCS-ineligible populations. LUAD: Lung adenocarcinoma; FHC: family history of cancer; PHC: personal history of cancer; yo: years old

CONCLUSIONS

- LCS current criteria exclude a significant proportion of individuals that will develop NSCLC.
- FHC may help to identify a high risk-population in LCS-ineligible group, particularly in non-smokers which may benefit of LCS.
- A deeper characterization of this population is currently being developed in a wider cohort (LAPIN study; EU4H-2024-PJ-04)

REFERENCES:

1. *Aberle et al. NEJM. 2011*
2. *De Koning et al. NEJM 2020.*
3. *Nandakumar et al. Eur Respir J. 2023*

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