

LUng Cancer-related risk factors and their Impact Assessment

### HORIZON-MISS-2021-CANCER-02

LUCIA Workshop – Understanding Lung Cancer San Sebastian, Sept. 5<sup>th</sup>, 2023

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# HISTOLOGICAL SUBTYPES AND MOLECULAR ANALYSIS OF LUNG CANCER

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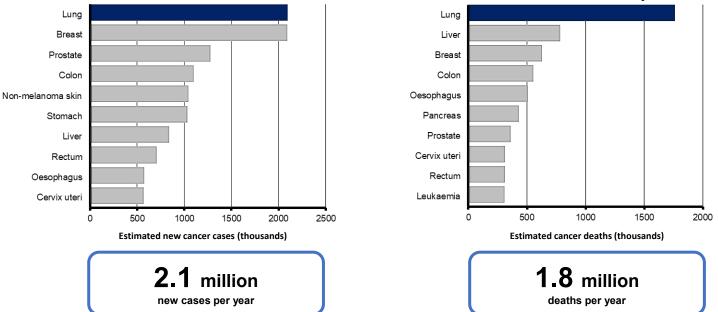




Worldwide annual incidence

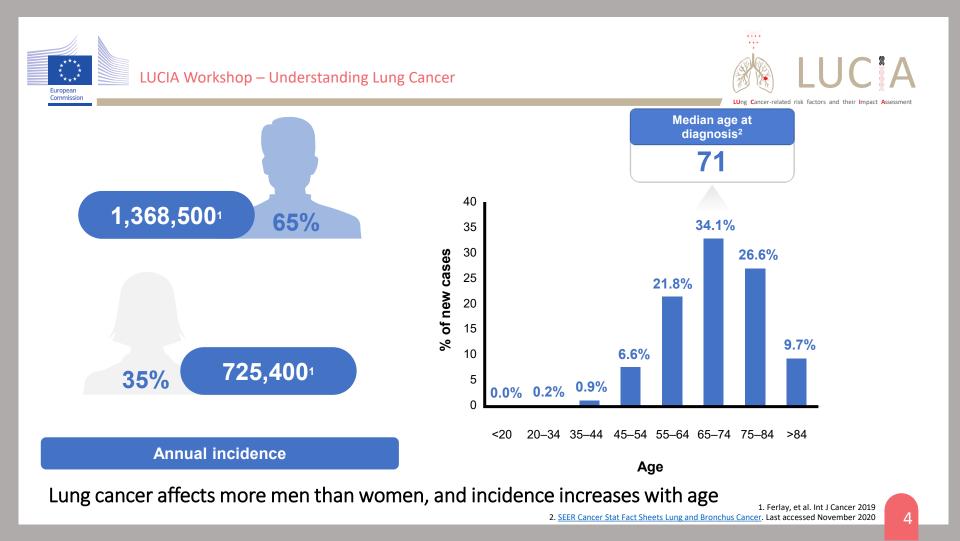


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Lung cancer has been the most common cancer in the world for several decades and remains the leading cause of cancer-related deaths

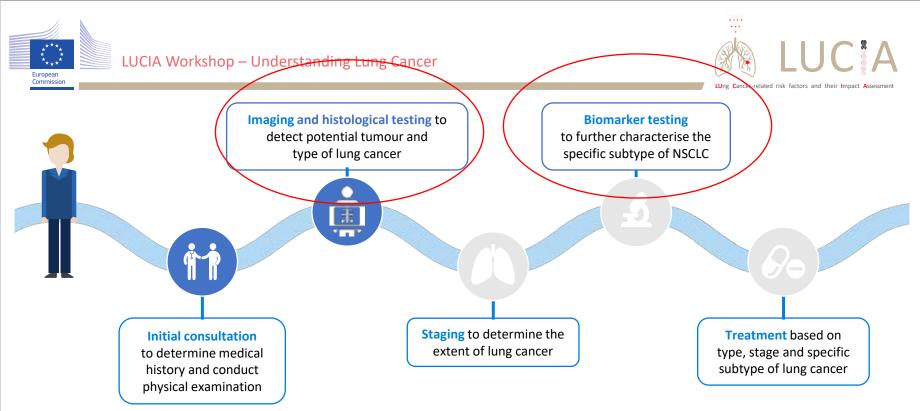
Worldwide annual mortality





LUng Cancer-related risk factors and their Impact Assessment 79% patients initially present **Overall 5 year survival** 5-year survival with regional or metastatic disease by disease type (all types) \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\* 20.5% \*\*\*\*\*\*\*\*\*\*\*\*\*\*\* 59.0% 31.7% \*\*\*\* 5.8% \*\*\*\* Regional Localised Metastatic (early/locally (advanced) (early) \*\*\*\*\*\*\*\*\*\*\*\* advanced) confined to spread to cancer has primary site regional metastasised lymph nodes to other organs

> The majority of lung cancer patients initially present with regional or metastatic disease and this significantly and adversely affects their survival outcomes



Typical patient journey from diagnosis to treatment

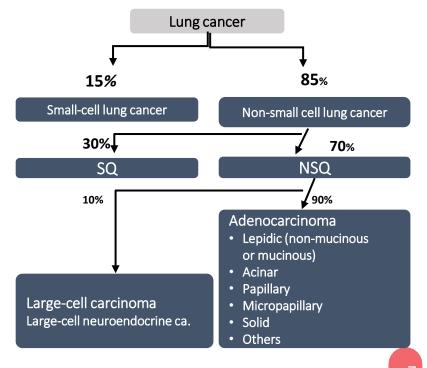
Accurate diagnosis enables the right treatment decision for the patient





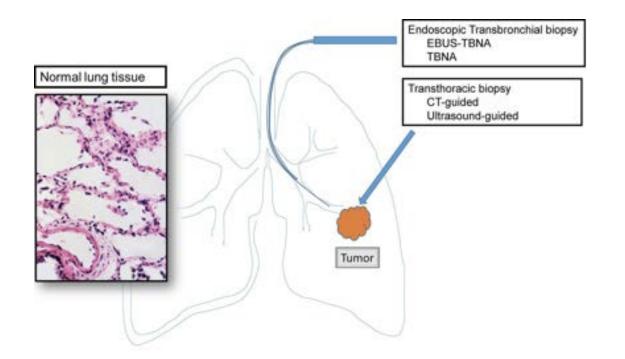
### **Histological subtypes**

- Small cell lung cancer (SCLC, 15%) and nonsmall cell lung cancer (NSCLC, 85%)
- NSCLC: heterogeneous disease that can be divided into four main subtypes: adenocarcinoma, SQ-cell carcinoma, largecell carcinoma and others (neuroendocrine, sarcomatoid...)





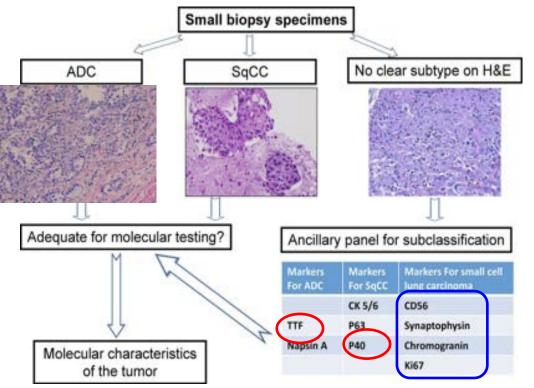








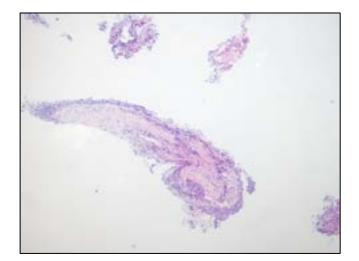
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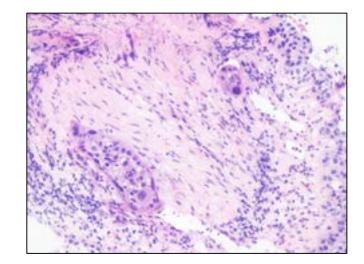






• Small diagnostic sample (broncoscopy biopsy)

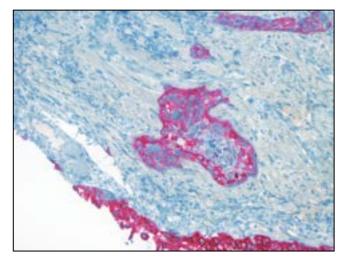


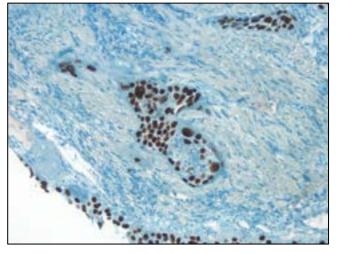






• Small diagnostic sample (broncoscopy biopsy)





TTF1-CK7

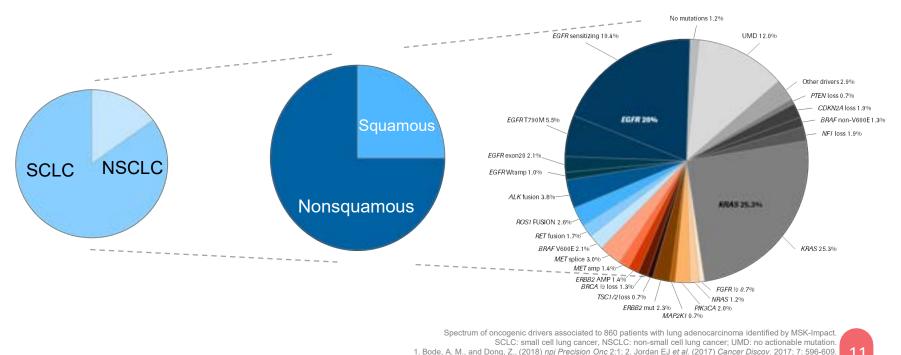
### p40-CK5/6



LUCA

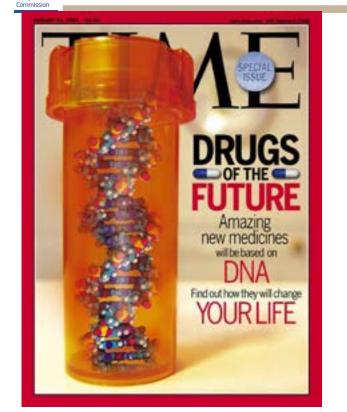
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### **Molecular subgroups and emerging therapies**





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### **Personalized Medicine**

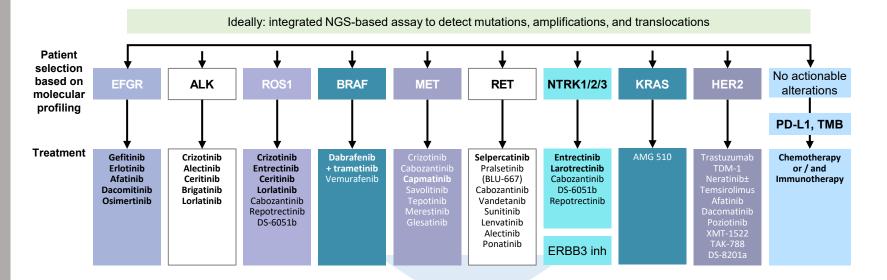
### The ability to offer

- The Right Drug
- To The Right Patient
- For The Right Disease
- At The Right Time
- With The Right Dosage





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Therapy switch/combination based on re-biopsies or liquid biopsy

\*Bold text = approved FDA and/or EU as of May 2020

• Rosell and Karachaliou. Lancet 2016

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Clinical and Translational Oncology https://doi.org/10.1007/s12094-022-03046-9

SPECIAL ARTICLE



New update to the guidelines on testing predictive biomarkers in non-small-cell lung cancer: a National Consensus of the Spanish Society of Pathology and the Spanish Society of Medical Oncology

Dolores Isla<sup>1</sup> · Maria D. Lozano<sup>2</sup> · Luis Paz-Ares<sup>3</sup> · Clara Salas<sup>4</sup> · Javier de Castro<sup>5</sup> · Esther Conde<sup>6</sup> · Enriqueta Felip<sup>7</sup> · Javier Gómez-Román<sup>8</sup> · Pilar Garrido<sup>9</sup> · Ana Belén Enguita<sup>10</sup>

Non-small cell lung cancer (NSCLC) is a group of tumours with the greatest number of identified therapeutic targets, some of which have clinical utility from the earliest stages





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Table 1 Essential biomarkers in NSCLC patients	Gene/protein	Predictive alteration	Methodology
	BGFR	Mutation	PCR: Sanger sequencing, real-time PCR and NGS
	AL.K	Rearrangement	IHC, FISH, real-time PCR and NGS
	ROST	Rearrangement	IHC (screening), FISH, real-time PCR and NGS
	BRAF V600	Mutation	Real-time PCR and NGS
	PD-L1	Overexpression	IHC
	NTRK	Rearrangement	IHC (screening), real-time PCR and NGS
	RET	Rearrangement	FISH, real-time PCR and NGS
	KRAS	Mutation	PCR: Sanger sequencing, real-time PCR and NGS
	MET	Mutation Amplification	NGS FISH, real-time PCR and NGS

ALK anaplastic lymphoma kinase, BRAF B-Raf proto-oncogene, EGFR epidermal growth factor receptor, FISH fluorescence in situ hybridisation, IHC immunohistochemistry, KRAS kirsten rat sarcoma virus, MET mesenchymal epithelial transition factor, NGS next-generation sequencing, NSCLC non-small cell lung cancer, NTRK neurotrophic tyrosine receptor kinase, PCR polymerase chain reaction, PD-LJ programmed death ligand-1, RET marranged during transfection, ROS1 c-ros oncogene 1

Table 2 Other biomarkers of interest in NSCLC patients		
Generprotein	Predictive alteration	Methodology
HER2	Metation Amplification	NGS FISH, stal-time PCR, NGS
TMB	Metations	NGS
STKIT	Metation	MGS-
KEAPI	Metation	NGS
MSI	Pattern of hypermatation	BIC, PCR, NGS

FISH fluorescence in situ hybridisation, HER2 human epidermal, growth factor receptor 2, JIIC immunohistochemistry, REAPT Kelchlike ECH-associated protein 1, MSI microsatellite instability-high, MGS next-generation sequencing, NSCLC non-small cell hang cancer, PCR polynetrase chain reaction, STR11 series/threonine kinase 11, TMR tumour mutation burden.





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