Supplementary Table 1: Histological classification of non-small cell lung cancer with clinical and pathological characteristics.

Subtype	Pathological features	Clinical information	Molecular profile/biomarkers	Therapeutic relevance
Adenocarcinoma (LUAD)	Glandular differentiation; mucin production; lepidic, papillary, or acinar growth patterns	Most common subtype (approximately 40–50%); more frequent in non-smokers, women, and younger patients; typically arises in peripheral lung regions	Frequent mutations: *EGFR*, *KRAS*, *ALK*, *ROS1*, *RET*, *NTRK* fusions; variable PD-L1 expression	Targeted therapies (EGFR-TKIs, ALK/ROS1 inhibitors); immunotherapy (PD-1/PD-L1 blockade); resistance via bypass signalling, EMT, and TME modulation
Squamous cell carcinoma (LUSC)	Keratinisation; intercellular bridges; polygonal cells	Accounts for approximately 25–30% of NSCLC; strongly associated with smoking; typically, central bronchial origin	Alterations in *FGFR1*, *DDR2*, *PIK3CA*; fewer actionable mutations; high TMB	Limited targeted therapy options: immunotherapy plays major role (PD-1/PD-L1 inhibitors); chemotherapy remains standard backbone
Large cell carcinoma (LCLC)	Undifferentiated morphology; large nuclei; prominent nucleoli; abundant cytoplasm	Less common (approximately 10–15%); aggressive behaviour; often diagnosed at	Lacks specific recurrent driver mutations; may overlap molecularly with LUAD or LUSC	Poor prognosis; managed with chemotherapy and immunotherapy; no established

		advanced stage		targeted therapies
Other rare variants (adenosquamous, sarcomatoid, neuroendocrine NSCLC)	Mixed histology or poorly differentiated features	Rare (<5% of NSCLC); often aggressive and resistant	May harbour mixed driver mutations; sarcomatoid often shows PD-L1 overexpression	Limited evidence base: immunotherapy may benefit subsets; clinical trials needed

ALK: anaplastic lymphoma kinase; EGFR: epidermal growth factor receptor; EMT: epithelial-mesenchymal transition; LCLC: large cell lung carcinoma; LUAD: lung adenocarcinoma; LUSC: lung squamous cell carcinoma; NSCLC: non-small cell lung cancer; PD-1: programmed death-1; PD-L1: programmed death-ligand 1; ROS1: ROS proto-oncogene 1, receptor tyrosine kinase; TKI: tyrosine kinase inhibitor; TMB: tumour mutational burden; TME: tumour microenvironment.